Proline-Catalyzed Asymmetric Addition Reaction of 9-Tosyl-3,4-dihydro- β -carboline with Ketones

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Supporting Information

General method

To the DMSO (0.8 ml) solution of 9-toluenesulfonyl-3,4-dihydro- β -carboline (1) (20.0 mg, 61.7 μ mol) was suspended (*S*)-proline (2.1 mg, 18.5 μ mol, 30 mol%). After cooling to -2°C, H₂O (55.5 μ l, 3.1 mmol) and a ketone (0.2 ml) was added to the mixture, and the reaction was continued for several hours. Then aqueous sat. NaHCO₃ was added to the mixture, which was extracted with CH₂Cl₂. The organic layer thus obtained was dried over MgSO₄ and evaporated off to leave a residue, which was chromatographed on silica gel to give the addition product.

(R)-1-[9-(Toluene-4-sulfonyl)-2,3,4,9-tetrahydro-1H- β -carbolin-1-yl]propan-2-one

Pale yellow amorphous. $[\alpha]_D^{21} = -189.66$ ($c=1.31$, MeOH); $t_r(S)=15.5$ min, $t_r(R)=20.6$ min, ee=93% (chiralcel OD, $\lambda=254$ nm, $iPrOH/hexane=1/1$); Anal. calcd for $C_{21}H_{22}N_2O_3S$: C, 65.95; H, 5.80; N, 7.32. Found: C, 65.93; H, 5.81; N, 7.28. 1H NMR (400 MHz, $CDCl_3$) δ : 2.26 (3H, s), 2.30 (3H, s), 2.61 (2H, t, $J=5.5$ Hz), 2.85 (1H, dd, $J=17.4, 9.9$ Hz), 2.99 - 3.11 (2H, m), 3.40 (1H, dd, $J=17.4, 2.0$ Hz), 4.99 (1H, d, $J=8.1$ Hz), 7.13 (1H, d, $J=8.6$ Hz), 7.23 (1H, td, $J=7.3, 0.9$ Hz), 7.30 (1H, td, $J=9.1, 1.7$ Hz), 7.32 (1H, d, $J=6.8$ Hz), 7.55 (2H, d, $J=8.4$ Hz), 8.14 (1H, dt, $J=8.4, 0.9$ Hz); ^{13}C NMR (100 MHz, $CDCl_3$) δ : 21.7, 22.5, 30.3, 37.5, 48.2, 49.1, 115.3, 118.2, 119.8, 123.8, 124.6, 126.2, 129.6, 130.4, 134.5, 136.3, 136.6, 144.6, 207.4.

(R)-1-[9-(Toluene-4-sulfonyl)-2,3,4,9-tetrahydro-1H- β -carbolin-1-yl]-butan-2-one

Pale yellow amorphous. $[\alpha]_D^{23} = -161.05$ ($c=0.85$, MeOH); $t_r(S)=13.7$ min, $t_r(R)=21.3$ min, ee=89% (chiralcel OD, $\lambda=254$ nm, $iPrOH/hexane=1/2$); HRMS (FAB⁺) m/z : Calcd for C₂₂H₂₅N₂O₃S (M+H)⁺ 397.1586, Found 397.1586; ¹H NMR (400 MHz, CDCl₃) δ : 1.05 (3H, t, $J=7.3$ Hz), 2.22 (3H, s), 2.38 – 2.58 (4H, m), 2.68 (1H, bs), 2.77 (1H, dd, $J=17.4, 9.7$ Hz), 2.92 – 3.06 (2H, m), 3.30 (1H, dd, $J=17.2, 1.8$ Hz), 4.95 (1H, d, $J=9.5$ Hz), 7.05 (2H, d, $J=8.1$ Hz), 7.16 (1H, td, $J=7.5, 1.1$ Hz), 7.20 – 7.26 (2H, m), 7.49 (2H, d, $J=8.4$ Hz), 8.06 (1H, d, $J=8.3$ Hz); ¹³C NMR (100 MHz, CDCl₃) δ : 7.6, 21.5, 22.2, 36.2, 37.3, 46.6, 49.0, 115.3, 118.4, 119.9, 123.9, 124.7, 126.4, 129.7, 130.5, 134.6, 136.3, 136.7, 144.8, 210.4.

(R)-1-[9-(Toluene-4-sulfonyl)-2,3,4,9-tetrahydro-1H- β -carbolin-1-yl]-pentan-2-one

Pale yellow amorphous. $[\alpha]_D^{23} = -165.14$ ($c=0.69$, MeOH); $t_r(S)=14.3$ min, $t_r(R)=21.9$ min, ee=92% (chiralcel OD, $\lambda=254$ nm, $iPrOH/hexane=1/2$); HRMS (FAB⁺) m/z : Calcd for C₂₃H₂₇N₂O₃S (M+H)⁺ 411.1742, Found 411.1745; ¹H NMR (400 MHz, CDCl₃) δ : 0.96 (3H, t, $J=7.5$ Hz), 1.68 (2H, sxt, $J=7.5$ Hz), 2.29 (3H, s), 2.33 – 2.59 (3H, m), 2.61 (2H, t, $J=4.9$ Hz), 2.83 (1H, dd, $J=17.4, 9.7$ Hz), 3.00 – 3.10 (2H, m), 3.37 (1H, dd, $J=17.2, 1.8$ Hz), 5.00 (1H, d, $J=8.3$ Hz), 7.12 (2H, d, $J=7.9$ Hz), 7.23 (1H, td, $J=7.3, 1.1$ Hz), 7.27 – 7.33 (3H, m), 7.56 (2H, d, $J=8.4$ Hz), 8.14 (1H, d, $J=7.3$ Hz); ¹³C NMR (100 MHz, CDCl₃) δ : 13.8, 17.2, 21.5, 22.4, 37.4, 45.0, 47.0, 49.0, 115.4, 118.3, 119.9, 123.9, 124.7, 126.4, 129.7, 130.6, 134.7, 136.6, 136.8, 144.8, 210.2.

(*R*)-4-Isobutoxy-1-[9-(toluene-4-sulfonyl)-2,3,4,9-tetrahydro-1H- β -carbolin-1-yl]-butan-2-one

Slightly yellow amorphous. $[\alpha]_D^{16} = -73.47$ ($c=1.17$, MeOH); $t_r=15.0$ min, 19.6 min, $ee=75\%$ (chiralcel OD, $\lambda=254$ nm, $iPrOH/hexane=1/1$); HRMS (FAB⁺) m/z : Calcd for $C_{26}H_{33}N_2O_4S$ ($M+H$)⁺ 469.2161, Found 469.2154; ¹H NMR (400 MHz, CDCl₃) δ : 0.89 (6H, d, $J=6.8$ Hz), 1.85 (1H, qui, $J=6.8$ Hz), 2.29 (3H, s), 2.47 (1H, brs), 2.61 (2H, t, $J=5.9$ Hz), 2.73 – 2.87 (2H, m), 2.93 (1H, dd, $J=17.4, 7.5$ Hz), 3.00 – 3.10 (2H, m), 3.20 (2H, d, $J=6.6$ Hz), 3.40 (1H, dd, $J=17.4, 2.0$ Hz), 3.74 (2H, td, $J=6.4, 2.8$ Hz), 5.03 (1H, d, $J=8.6$ Hz), 7.12 (2H, d, $J=8.1$ Hz), 7.21 – 7.55 (3H, m), 7.56 (2H, d, $J=6.6$ Hz), 8.14 (1H, d, $J=6.2$ Hz); ¹³C NMR (100 MHz, CDCl₃) δ : 19.3, 21.5, 22.2, 28.3, 37.1, 43.2, 47.5, 48.8, 65.8, 78.1, 115.3, 118.3, 119.8, 123.9, 124.7, 126.4, 129.7, 130.5, 134.7, 136.4, 136.7, 144.7, 208.5.

Reaction of 9-tosyl-3,4-dihydro-β-carboline (1) with 3-buten-2-one in the presence of (S)-proline

To the dry DMSO solution (65 ml) of compound 1 (211.7 mg, 0.65 mmol) and (S)-proline (37.6 mg, 0.33 mmol) was added methyl vinyl ketone (163.0 μ l, 1.96 mmol) at 20°C, and the mixture was allowed to react for 7 days at 20°C. Then dichloromethane was added, and the mixture was washed with saturated aqueous NaHCO₃ and brine, dried over MgSO₄, and evaporated off. The residue thus obtained was chromatographed on silica gel (ethyl acetate) to give (R)-12-tosyl-3,4,6,7,12,12b-hexahydro-1H-indolo[2,3-a]quinolizin-2-one (6).

(R)-12-tosyl-3,4,6,7,12,12b-hexahydro-1H-indolo[2,3-a]quinolizin-2-one

Pale yellow amorphous. $[\alpha]_D^{23} = -84.60$ ($c = 0.86$, CHCl₃), $t_r(S) = 19.5$ min, $t_r(R) = 26.8$ min, ee=92% (chiralcel OJ-H, $\lambda = 254$ nm, i PrOH/hexane=1/1); Anal. calcd for C₂₂H₂₂N₂O₃S: C, 66.98; H, 5.62; N, 7.10. Found: C, 66.79; H, 5.75; N, 6.82. ¹H-NMR (400 MHz, CDCl₃) δ : 2.33 (3H, s), 2.38 (1H, dt, $J = 15.0, 1.7$ Hz), 2.54 (1H, dd, $J = 14.7, 11.4$ Hz),

2.66 – 2.91 (4H, m), 3.25 – 3.31 (2H, m), 3.35 (1H, dt, $J=14.5, 2.8$ Hz), 3.44 (1H, ddd, $J=13.2, 7.2, 1.7$ Hz), 4.51 (1H, d, $J=11.4$ Hz), 7.10 (2H, d, $J=8.1$ Hz), 7.23 (1H, td, $J=7.3, 0.9$ Hz), 7.29 (1H, td, $J=8.4, 1.7$ Hz), 7.49 (2H, d, $J=8.6$ Hz), 8.08 (1H, d, $J=8.3$ Hz); ^{13}C NMR (100 MHz, CDCl_3) δ : 21.7, 22.5, 38.8, 45.6, 45.8, 53.6, 58.1, 115.8, 118.4, 119.7, 124.0, 124.8, 126.3, 129.4, 130.2, 134.1, 135.9, 137.4, 144.5.

To the THF solution (2.0 ml) of the starting material (30.3 mg, 76.6 μmol) was added tetra-*n*-butylammonium fluoride 1.0 M solution in THF (460 ml, 460 μmol) at room temperature, and the mixture was allowed to react under reflux for 1.5 h. Then sat. NaHCO_3 aqueous solution was added, and the mixture was extracted with CH_2Cl_2 . The organic layer was washed with brine, dried over MgSO_4 , and evaporated off to leave a residue, which was chromatographed on silica gel (AcOEt) to give the product (13.6 mg, 74%).

(R)-3,4,6,7,12,12b-hexahydro-1H-indolo[2,3-a]quinolizin-2-one

Slightly yellow amorphous. $[\alpha]_D^{18} = +85.3$ ($c=0.62$, CH_2Cl_2), *lit. $[\alpha]_D^{18} = +44.5$ ($c=1.1$, CH_2Cl_2 , enantiomeric purity ca 3-4 : 1); HRMS (FAB^+) m/z : Calcd for $\text{C}_{15}\text{H}_{17}\text{N}_2\text{O}$ ($\text{M}+\text{H}^+$) 241.1341, Found 241.1341; ^1H -NMR (400 MHz, CDCl_3) δ : 2.50 (1H, d, $J=11.4$ Hz), 2.64 (1H, t, $J=12.1$ Hz), 2.71 – 2.85 (5H, m), 3.02 – 3.09 (1H, m), 3.27 (1H, dd, $J=11.4$, 5.6 Hz), 3.31 – 3.36 (1H, m), 3.68 (1H, d, $J=11.9$ Hz), 7.12 (1H, td, $J=7.0$, 1.1 Hz), 7.17 (1H, td, $J=7.0$, 1.1 Hz), 7.33 (1H, d, $J=7.9$ Hz), 7.50 (1H, d, $J=7.7$ Hz), 7.88 (1H, brs); ^{13}C NMR (100 MHz, CDCl_3) δ : 21.6, 41.5, 45.6, 51.9, 53.4, 54.1, 58.5, 108.5, 111.0, 118.2, 118.3, 119.7, 121.9, 126.9, 132.8, 136.2, 207.5.

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The allyl adduct (360.0 mg, 1.7 mmol) was dissolved in dry CH_2Cl_2 (7.0 ml), and Et_3N (710 μl , 5.1 mmol) and AcCl (242.0 μl , 3.4 mmol) were successively added to the solution at 0°C under Ar. After the reaction continued for another 2 h at room

temperature, sat. NaHCO₃ aqueous solution was added to the mixture. Then the mixture was extracted with CH₂Cl₂, and the organic layer thus obtained was dried over MgSO₄, and evaporated off. The residue was separated on NH-SiO₂ column (AcOEt) to give the product (421.2 mg) in 98% yield.

(S)-1-(1-Allyl-1,3,4,9-tetrahydro- β -carbolin-2-yl)-ethanone

Pale yellow crystal. $[\alpha]_D^{23} = +109.15$ (c=1.07, MeOH), $t_r(R) = 14.5$ min, $t_r(S) = 15.5$ min, ee=92% (chiralcel OD, $\lambda = 254$ nm, *i*PrOH/hexane=1/1); Anal. calcd for C₁₆H₁₈N₂O: C, 75.56; H, 7.13; N, 11.01. Found: C, 75.29; H, 7.31; N, 10.75. The product was obtained as a mixture of two conformational isomers (1:0.3). The NMR spectra of the major isomer are shown; ¹H-NMR (400 MHz, CDCl₃) δ : 3.23 (3H, s), 2.60 (2H, td, $J = 7.0, 1.1$ Hz), 2.82 (2H, dd, $J = 5.9, 3.5$ Hz), 3.51 (1H, ddd, $J = 13.9, 10.5, 5.5$ Hz), 4.02 (1H, ddd, $J = 13.8, 4.6, 1.7$ Hz), 5.12 (1H, s), 5.16 (1H, d, $J = 3.7$ Hz), 5.78 (1H, t, $J = 7.0$ Hz), 5.97 (1H, dq, $J = 17.2, 7.3$ Hz), 7.08 – 7.18 (2H, m), 7.23 (1H, d, $J = 8.1$ Hz), 7.47 (1H, d, $J = 7.9$ Hz), 8.15 (1H, drs); ¹³C NMR (100 MHz, CDCl₃) δ : 21.9, 38.7, 41.4, 48.7, 53.8, 107.6, 111.0, 117.8, 118.1, 119.3, 121.6, 126.4, 133.9, 134.4, 136.0, 169.6.

To the NaH (43.5 mg, 1.09 mmol) suspension in THF (13.0 ml) was added the starting material (184.0 mg, 724.4 μ mol) under Ar at 0°C, then the mixture was allowed to react for 10 min. Then *p*-toluenesulfonyl chloride (276.2 mg, 1.45 mmol) was added, and the reaction was continued for 23 h. After the addition of 0.2 N HCl, the mixture was extracted with CH₂Cl₂, which was dried over MgSO₄ and evaporated off to leave a residue. The residue was chromatographed on silica gel (10% AcOEt in CH₂Cl₂) to give the product (133.9 mg, 45.3%) accompanied with the recovery of the starting material (80.1 mg, 43.5%).

(S)-1-[1-Allyl-9-(toluene-4-sulfonyl)-1,3,4,9-tetrahydro- β -carbolin-2-yl]-ethanone

Slightly yellow amorphous. $[\alpha]_D^{23} = +169.12$ ($c=0.97$, MeOH), $t_r(S)=17.5$ min, $t_r(R)=18.9$ min, ee=92% (chiralcel OD, $\lambda=254$ nm, *i*PrOH/hexane=1/5); HRMS (FAB⁺) m/z : Calcd for C₂₃H₂₅N₂O₃S (M+H)⁺ 409.1586, Found 409.1559; Since the product was obtained as a mixture of two conformational isomers (1:0.9), it is difficult to distinguish major one from another. But the addition of a little amount of TFA changes the ratio to 1:0.6. The NMR spectra of the major isomer in the presence of TFA are shown;

$^1\text{H-NMR}$ (400 MHz, CDCl_3) δ : 2.28 (3H, s), 2.32 (3H, s), 2.44 – 2.63 (1H, m), 2.71 – 2.80 (1H, m), 3.27 (1H, brd, $J=14.7$ Hz), 3.62 (1H, dt, $J=13.7, 9.2$ Hz), 4.00 (1H, dt, $J=14.1, 2.9$ Hz), 5.09 (1H, brs), 5.12 (1H, d, $J=10.6$ Hz), 5.84 – 5.96 (1H, m), 5.63 (1H, dd, $J=10.8, 3.1$ Hz), 7.15 (2H, d, $J=8.3$ Hz), 7.24 – 7.37 (3H, m), 7.68 (2H, d, $J=8.4$ Hz), 8.21 (1H, d, $J=8.3$ Hz); $^{13}\text{C NMR}$ (100 MHz, CDCl_3) δ : 21.5, 21.6, 35.4, 39.2, 50.6, 70.6, 113.0, 115.6, 118.0, 118.5, 119.0, 124.3, 125.5, 126.7, 129.4, 130.0, 132.5, 134.0, 136.7, 145.5, 173.4.

To the acetone (6.0 ml)/ H_2O (12 ml) solution of N-methylmorpholine (50wt.% sol. in H_2O) (483.5 μl , 2.06 mmol) was added OsO_4 (4 wt.% sol. in H_2O) (218.5 μl , 34.4 μmol). Then the acetone solution (18 ml) of the starting material (280.6 mg, 687.7 μmol) was added, and the mixture was allowed to react for 8.5 h under Ar. After the addition of 10% NaHSO_3 aqueous solution (12 ml) and 1 h's stirring, the mixture was extracted with AcOEt . The organic layer was dried over MgSO_4 , and evaporated off to leave a residue, which was dissolved in acetone (12 ml). To the acetone solution was added 7% NaIO_4 aqueous solution (2.1 ml, 687.7 μmol), and the mixture was allowed to react for 10 h. After the addition of water, the mixture was extracted with CH_2Cl_2 , and the obtained organic layer was dried over MgSO_4 , and evaporated. A residue thus formed was chromatographed on silica gel (20% AcOEt in CH_2Cl_2) to give the product (216.8 mg, 76.9%).

(S)-[2-Acetyl-9-(*p*-toluenesulfonyl)-2,3,4,9-tetrahydro-1H- β -carbolin-1-yl]acetaldehyde

Slightly yellow amorphous. $[\alpha]_D^{23} = +308.52$ ($c = 0.87$, CHCl_3); HRMS (FAB^+) m/z : Calcd for $\text{C}_{22}\text{H}_{23}\text{N}_2\text{O}_4\text{S}$ ($\text{M} + \text{H}^+$) 411.1379, Found 411.1346; The product was obtained as a mixture of two conformational isomers (1:0.4). The NMR spectra of the major isomer are shown; ^1H -NMR (400 MHz, CDCl_3) δ : 2.19 (3H, s), 2.29 (3H, s), 2.65 – 2.75 (3H, m), 3.44 (1H, ddd, $J = 14.9, 7.7, 1.7$ Hz), 3.50 (1H, dd, $J = 15.4, 2.8$ Hz), 3.99 (1H, dt, $J = 14.5, 3.7$ Hz), 7.04 (1H, d, $J = 10.5$ Hz), 7.17 (2H, d, $J = 8.1$ Hz), 7.23 – 7.39 (3H, m), 7.73 (2H, d, $J = 8.4$ Hz), 8.18 (1H, d, $J = 8.2$ Hz), 9.89 (1H, d, $J = 5.0$ Hz); ^{13}C NMR (100 MHz, CDCl_3) δ : 21.5, 21.7, 38.8, 45.0, 48.9, 49.1, 115.4, 118.4, 124.2, 125.3, 126.8, 129.6, 129.9, 133.9, 134.1, 136.6, 145.1, 169.9, 200.4.

To the dry THF solution (6.0 ml) of the starting material was added MeMgBr (3.0 M sol. in Et_2O) (120.0 μl , 360.0 μmol) at 0°C under Ar, and the mixture was allowed to react

for 17 h under ambient temperature. After cooling to 0°C, saturated NH₄Cl aqueous solution was added, and the mixture was extracted with CH₂Cl₂. The organic layer was dried over MgSO₄, and evaporated off to leave a residue, which was chromatographed on silica gel (AcOEt) to give the product (43.5 mg, 85%) as a mixture of two diastereomers (3:1).

(S)-1-[1-(2-Hydroxypropyl)-9-(*p*-toluenesulfonyl)-1,3,4,9-tetrahydro-β-carbolin-2-yl]-ethanone

HRMS (FAB⁺) *m/z*: Calcd for C₂₃H₂₇N₂O₄S (M+H)⁺ 427.1692, Found 427.1682

To the dry DMSO solution (1.0 ml) of the starting material (9.8 mg, 23.0 μmol) was added acetic anhydride (0.7 ml) under Ar at room temperature, and the mixture was allowed to react for 18 h. Then sat.NaHCO₃ aqueous solution was added, and the mixture was extracted with CH₂Cl₂. The organic layer thus formed was dried over MgSO₄, and evaporated off to leave a residue, which was chromatographed on silica gel (AcOEt) to give the product (6.5 mg, 67%).

1-[2-Acetyl-9-(*p*-toluenesulfonyl)-2,3,4,9-tetrahydro- β -carbolin-1-yl]propan-2-one

Slightly yellow amorphous. $[\alpha]_D^{23} = +187.10$ ($c=1.05$, MeOH), $t_r(S)=16.7$ min, $t_r(R)=20.3$ min, ee=89% (chiralcel OD, $\lambda=254$ nm, *i*PrOH/hexane=1/3); HRMS (FAB⁺) m/z : Calcd for $C_{23}H_{25}N_2O_4S$ ($M+H$)⁺ 425.1535, Found 425.1566; The product was obtained as a mixture of two conformational isomers (1:0.6). The NMR spectra of the major isomer are shown; ¹H-NMR (400 MHz, CDCl₃) δ : 2.18 (3H, s), 2.29 (3H, s), 2.44 (3H, s), 2.54 – 2.89 (3H, m), 3.49 – 3.56 (1H, m), 3.58 (1H, dd, $J=10.5, 2.9$ Hz), 3.96 (1H, dt, $J=14.7, 3.5$ Hz), 6.98 (1H, dd, $J=11.6, 2.8$ Hz), 7.17 (2H, d, $J=8.1$ Hz), 7.22 – 7.38 (3H, m), 7.75 (2H, d, $J=8.6$ Hz), 8.17 (1H, d, $J=8.3$ Hz); ¹³C NMR (100 MHz, CDCl₃) δ : 21.5, 21.6, 21.7, 29.1, 38.5, 46.5, 48.8, 115.4, 118.4, 118.7, 124.1, 125.2, 126.8, 129.6, 129.8, 134.1, 134.6, 136.5, 145.0, 169.9, 207.1

To the dry THF solution (5.0 ml) of the starting material (45.9 mg, 1120.0 μmol) was added EtMgBr (1.0 M sol. in THF) (335.9 μl , 335.9 μmol) at 0°C under Ar, and the mixture was allowed to react at ambient temperature for 23 h. After cooling, sat.NH₄Cl aqueous solution was added, and the mixture was extracted with CH₂Cl₂. The residue thus obtained was dissolved in dry DMSO (4.0 ml), and acetic anhydride (2.8 ml) was added dropwise under Ar at room temperature. The reaction was continued for 19 h, and stopped by the addition of sat.NaHCO₃ aqueous solution. The mixture thus obtained was extracted with CH₂Cl₂, and the organic layer was dried over MgSO₄, and evaporated off to leave a residue, which was chromatographed on silica gel (AcOEt) to give the product (35.5 mg, 72%).

(S)-1-[2-Acetyl-9-(*p*-toluenesulfonyl)-2,3,4,9-tetrahydro- β -carbolin-1-yl]butan-2-one

Slightly yellow amorphous. $[\alpha]_D^{23}=194.90$ ($c=1.22$, MeOH); $t_r(S)=14.7$ min, $t_r(R)=16.2$ min, ee=90% (chiralcel OD, $\lambda=254$ nm, *i*PrOH/hexane=1/2); HRMS (FAB⁺) m/z : Calcd for C₂₄H₂₇N₂O₄S (M+H)⁺ 439.1692, Found 439.1701; The product was obtained as a mixture of two conformational isomers (1:0.6). The NMR spectra of the major isomer are shown; ¹H NMR (400 MHz, CDCl₃) δ : 1.09 (3H, t, $J=7.3$ Hz), 2.27 (3H, s), 2.29 (3H, s), 2.53 – 2.83 (5H, m), 3.58 (2H, dt, $J=12.7, 9.2$ Hz), 3.96 (1H, dt, $J=14.3, 3.5$ Hz), 4.78 (1H, dd, $J=13.0, 5.7$ Hz), 7.17 (2H, d, $J=8.1$ Hz), 7.22 – 7.38 (3H, m), 7.75 (2H, d,

$J=8.4$ Hz), 8.17 (1H, d, $J=8.4$ Hz); ^{13}C NMR (100 MHz, CDCl_3) δ : 7.6, 21.5, 21.6, 21.7, 34.8, 38.5, 47.3, 47.4, 115.4, 118.4, 119.9, 124.0, 125.1, 126.8, 129.4, 129.7, 129.8, 134.1, 134.8, 136.5, 145.0, 169.7, 209.4.

To the dry CH₂Cl₂ solution (2.0 ml) of the starting material were added Et₃N (21.0 μl, 152.4 μmol) and AcCl (7.2 μl, 101.6 μmol) successively at 0°C under Ar atmosphere, and the mixture was allowed to react for 1 h at room temperature. After the addition of water at 0°C, the mixture was extracted with CH₂Cl₂. The organic layer thus obtained was dried over MgSO₄, and evaporated off to leave a residue, which was chromatographed on silica gel (50% AcOEt in CH₂Cl₂) to give the product (21.0 mg, 97.5 %).

(R)-1-[2-Acetyl-9-(*p*-toluenesulfonyl)-2,3,4,9-tetrahydro-β-carboline-1-yl]propan-2-one.

$[\alpha]_{\text{D}}^{23} = -195.52$ ($c=1.05$, MeOH), $t_{\text{r}}(\text{S})=16.7$ min, $t_{\text{r}}(\text{R})=20.3$ min, ee=93% (chiralcel OD, $\lambda=254$ nm, *i*PrOH/hexane=1/3)

To the DMSO (0.8 ml) solution of 9-toluenesulfonyl-3,4-dihydro-β-carboline (**1**) (35.4 mg, 109.3 μmol) was suspended (*S*)-proline (3.8 mg, 32.8 μmol, 50 mol%). Then H₂O (98 μl, 3.5 mmol) and 2-butanone (0.3 ml) were successively added, and the mixture was allowed to react at -2°C for 4.5 h. After quenching with sat. NaHCO₃ aqueous solution, the mixture was extracted with CH₂Cl₂. The organic layer was washed with H₂O, dried over MgSO₄, and evaporated off. The residue thus obtained was dissolved in dry CH₂Cl₂ (2.0 ml), then Et₃N (46.0 μl, 327.8 μmol) and acetyl chloride (15.5 μl, 218.5 μmol) was added in series at 0°C. The reaction was continued for another 30 min before quenching with H₂O at 0°C. The mixture was extracted with CH₂Cl₂, which was dried over MgSO₄, and evaporated. The residue thus obtained was chromatographed on silica gel (AcOEt) to give the product (33.5 mg, 72%).

(*R*)-1-[2-Acetyl-9-(toluene-4-sulfonyl)-2,3,4,9-tetrahydro-β-carbolin-1-yl]butan-2-one.

Slightly yellow amorphous. $[\alpha]_D^{23} = -189.52$ ($c = 0.91$, MeOH); $t_R(S) = 14.3$ min, $t_R(R) = 16.2$ min, ee = 89% (chiralcel OD, $\lambda = 254$ nm, $i\text{PrOH/hexanes} = 1/2$)