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

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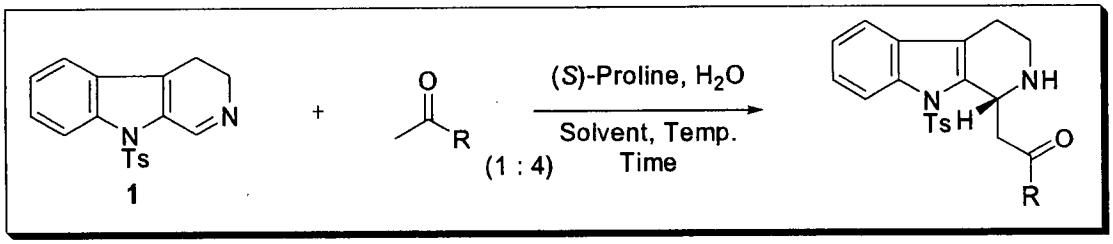
Supporting Information



General method

To the DMSO (0.8 ml) solution of 9-toluenesulfonyl-3,4-dihydro-β-carboline (**1**) (20.0 mg, 61.7 μmol) was suspended (*S*)-proline (2.1 mg, 18.5 μmol, 30 mol%). After cooling to -2°C, H_2O (55.5 μl, 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. $NaHCO_3$ was added to the mixture, which was extracted with CH_2Cl_2. The organic layer thus obtained was dried over $MgSO_4$ and evaporated off to leave a residue, which was chromatographed on silica gel to give the addition product.

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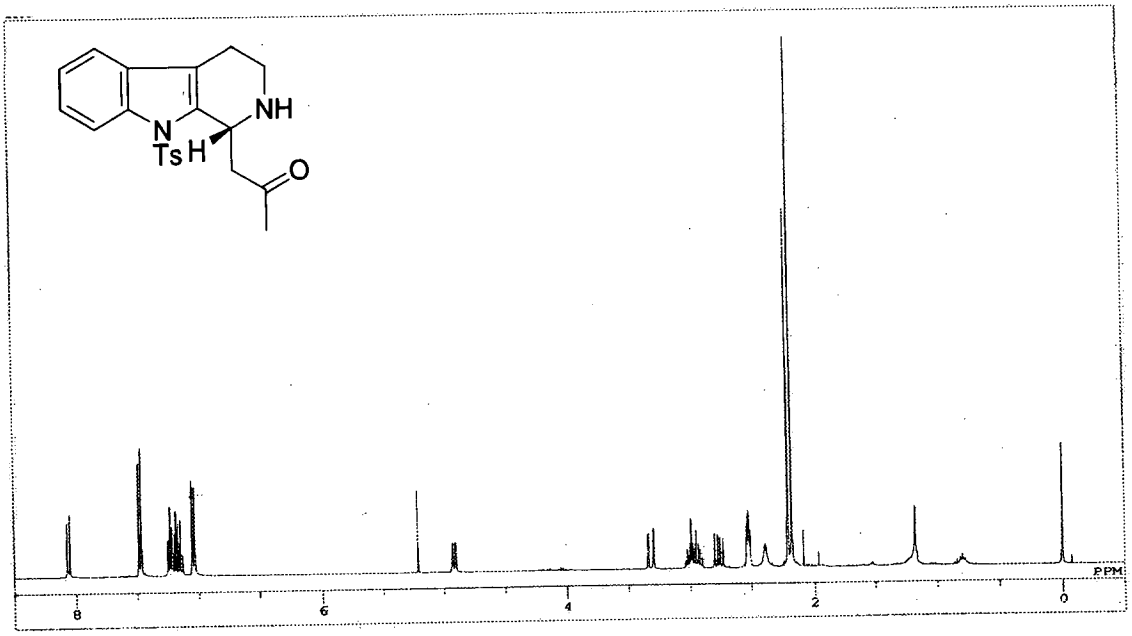
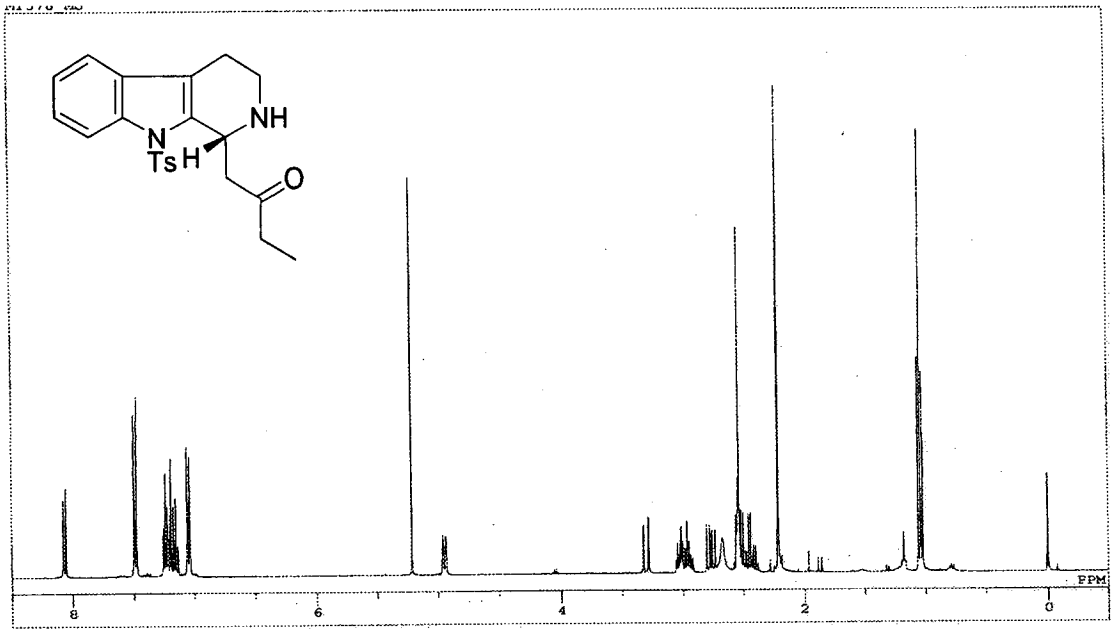
(*R*)-1-[9-(Toluene-4-sulfonyl)-2,3,4,9-tetrahydro-1H-β-carbolin-1-yl]propan-2-one



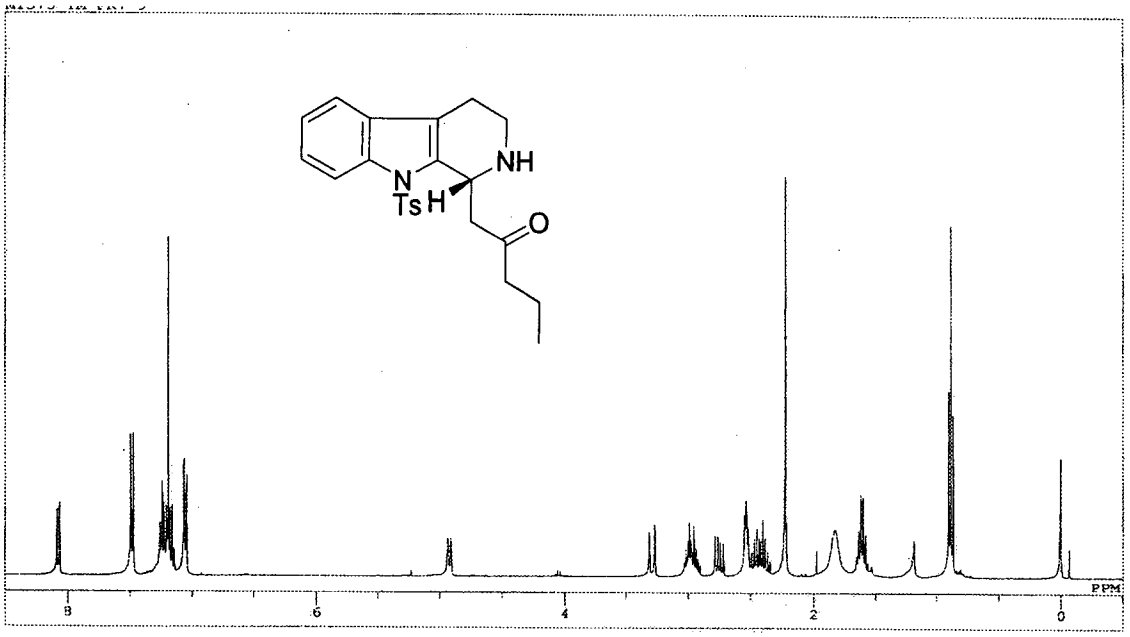
Pale yellow amorphous. $[\alpha]^{21}_{D}$=-189.66 (c=1.31, MeOH); t_r(*S*)=15.5 min, t_r(*R*)=20.6 min, ee=93% (chiralcel OD, λ=254 nm, *i*PrOH/hexane=1/1); Anal. calcd for $C_{21}H_{22}N_2O_3S$: C, 65.95; H, 5.80; N, 7.32. Found: C, 65.93; H, 5.81; N, 7.28. ^{1}H NMR (400 MHz, $CDCl_3$) δ: 2.26 (3H, 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



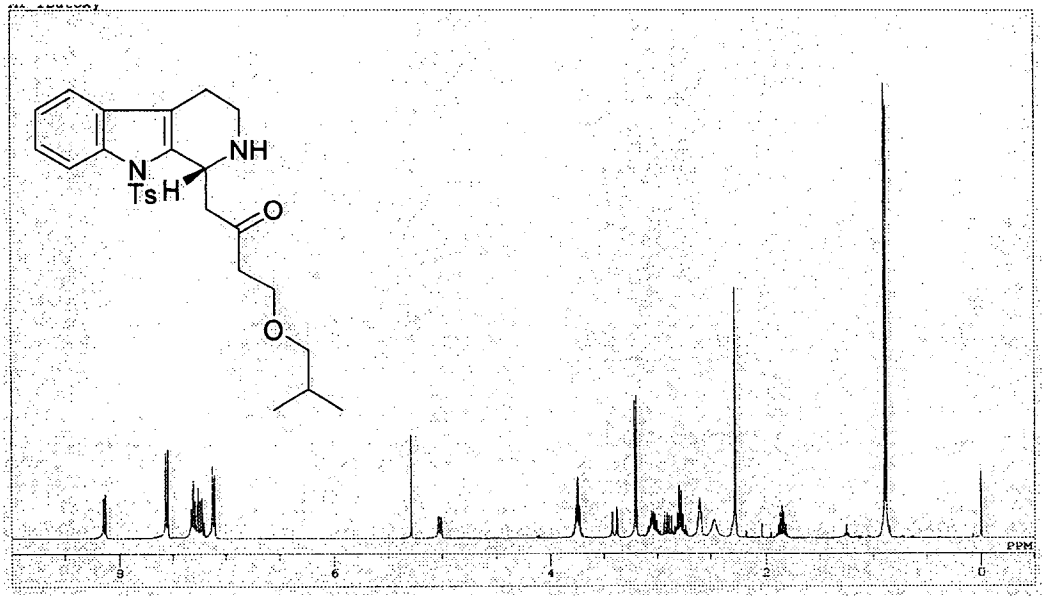
Pale yellow amorphous. $[\alpha]^{23}_{D}$=-161.05 (c=0.85, MeOH); t_r(*S*)=13.7 min, t_r(*R*)=21.3 min, ee=89% (chiralcel OD, λ=254 nm, *i*PrOH/hexane=1/2); HRMS (FAB$^+$) *m/z*: Calcd for $C_{22}H_{25}N_2O_3S$ $(M+H)^+$ 397.1586, Found 397.1586; ^{1}H NMR (400 MHz, $CDCl_3$) δ: 1.05 (3H, t, *J*=7.3 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); ^{13}C NMR (100 MHz, $CDCl_3$) 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

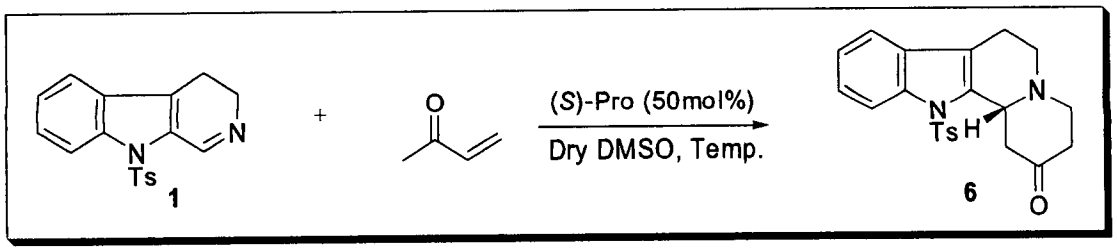


Pale yellow amorphous. $[\alpha]^{23}_{D}$=-165.14 (c=0.69, MeOH); t_r(*S*)=14.3 min, t_r(*R*)=21.9 min, ee=92% (chiralcel OD, λ=254 nm, *i*PrOH/hexane=1/2); HRMS (FAB$^+$) *m/z*: Calcd for $C_{23}H_{27}N_2O_3S$ $(M+H)^+$ 411.1742, Found 411.1745; ^{1}H NMR (400 MHz, $CDCl_3$) δ: 0.96 (3H, t, *J*=7.5 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); ^{13}C NMR (100 MHz, $CDCl_3$) 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



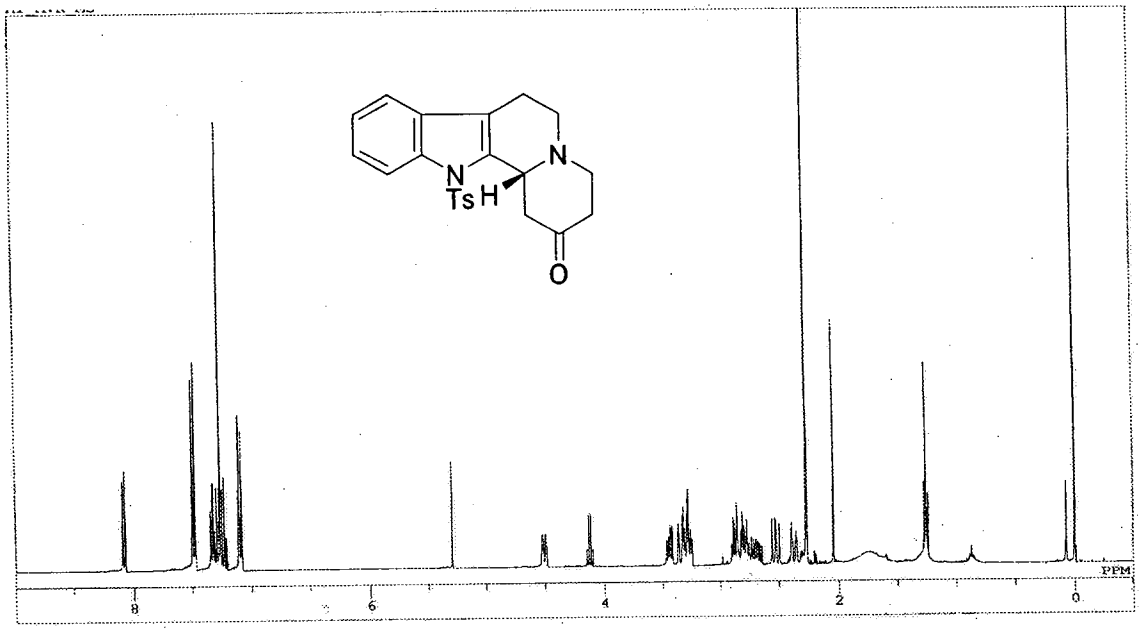
Slightly yellow amorphous. $[\alpha]^{16}_{D}$=-73.47 (c=1.17, MeOH); t_r=15.0 min, 19.6 min, ee=75% (chiralcel OD, λ=254 nm, *i*PrOH/hexane=1/1); HRMS (FAB$^+$) *m/z*: Calcd for $C_{26}H_{33}N_2O_4S$ $(M+H)^+$ 469.2161, Found 469.2154; ^{1}H NMR (400 MHz, $CDCl_3$) δ: 0.89 (6H, d, *J*=6.8 Hz), 1.85 (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); ^{13}C NMR (100 MHz, $CDCl_3$) 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

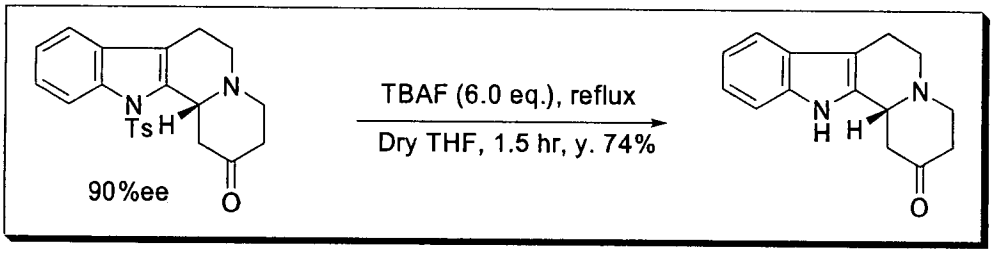
To the dry DMSO solution (65 ml) of compound **1** (211.7 mg, 0.65 mmol) and (*S*)-proline (37.6 mg, 0.33 mmol) was added methyl vinyl ketone (163.0 μl, 1.96 mmol) at 20°C, and the mixture was allowed to react for 7 days at 20°C. Then dichloromethane was added, and the mixture was washed with saturated aqueous $NaHCO_3$ and brine, dried over $MgSO_4$, 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-1*H*-indolo[2,3-*a*]quinolizin-2-one (**6**).

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



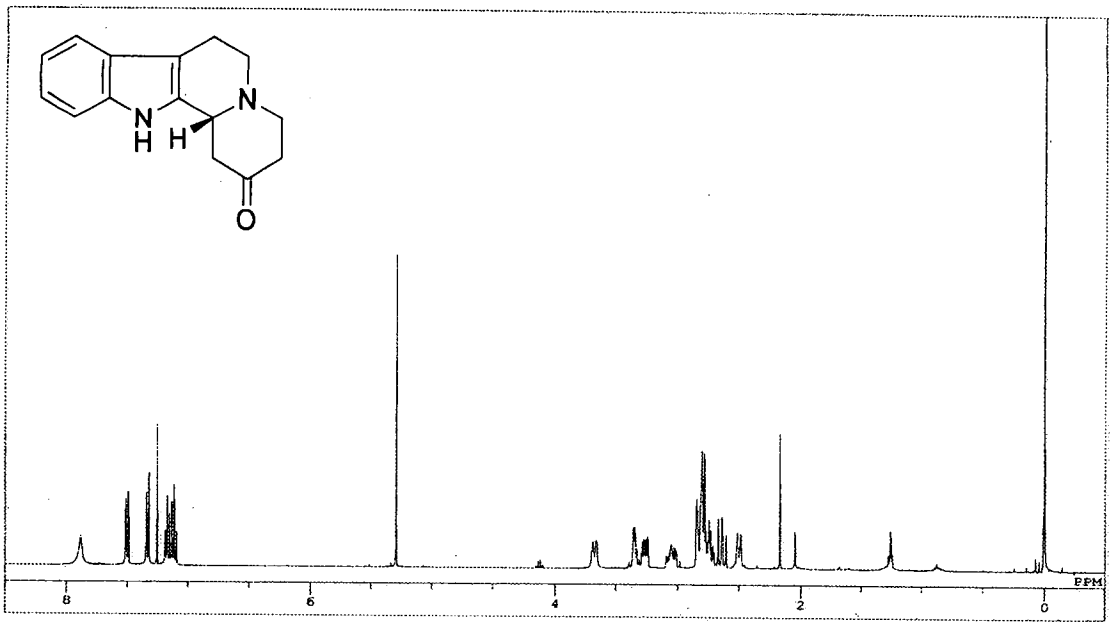
Pale yellow amorphous. $[\alpha]^{23}_D$=-84.60 (c=0.86, $CHCl_3$), t_r(*S*)=19.5 min, t_r(*R*)=26.8 min, ee=92% (chiralcel OJ-H, λ=254 nm, *i*PrOH/hexane=1/1); Anal. calcd for $C_{22}H_{22}N_2O_3S$: C, 66.98; H, 5.62; N, 7.10. Found: C, 66.79; H, 5.75; N, 6.82. ^{1}H-NMR (400 MHz, $CDCl_3$) δ: 2.33 (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.



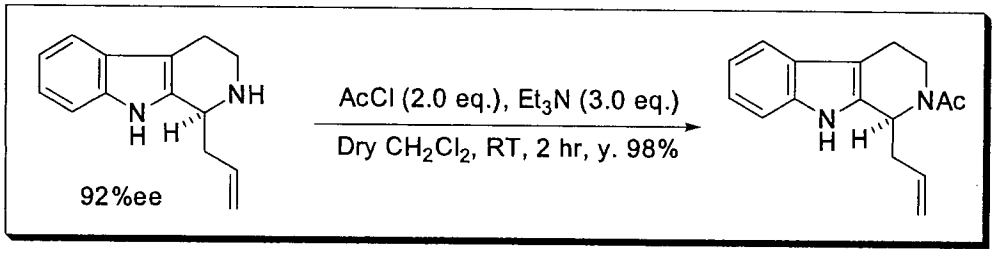
To the THF solution (2.0 ml) of the starting material (30.3 mg, 76.6 μmol) was added tetra-n-butylammonium fluoride 1.0 M solution in THF (460 ml, 460 μmol) at room temperature, and the mixture was allowed to react under reflux for 1.5 h. Then sat. $NaHCO_3$ aqueous solution was added, and the mixture 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-1*H*-indolo[2,3-*a*]quinolizin-2-one



Slightly yellow amorphous. $[\alpha]^{18}_{D}$=+85.3 (c=0.62, CH_2Cl_2), *lit. $[\alpha]^{18}_{D}$=+44.5 (c=1.1, CH_2Cl_2, enantiomeric purity ca 3-4 : 1); HRMS (FAB$^+$) *m/z*: Calcd for $C_{15}H_{17}N_2O$ $(M+H)^+$ 241.1341, Found 241.1341; ^{1}H-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.

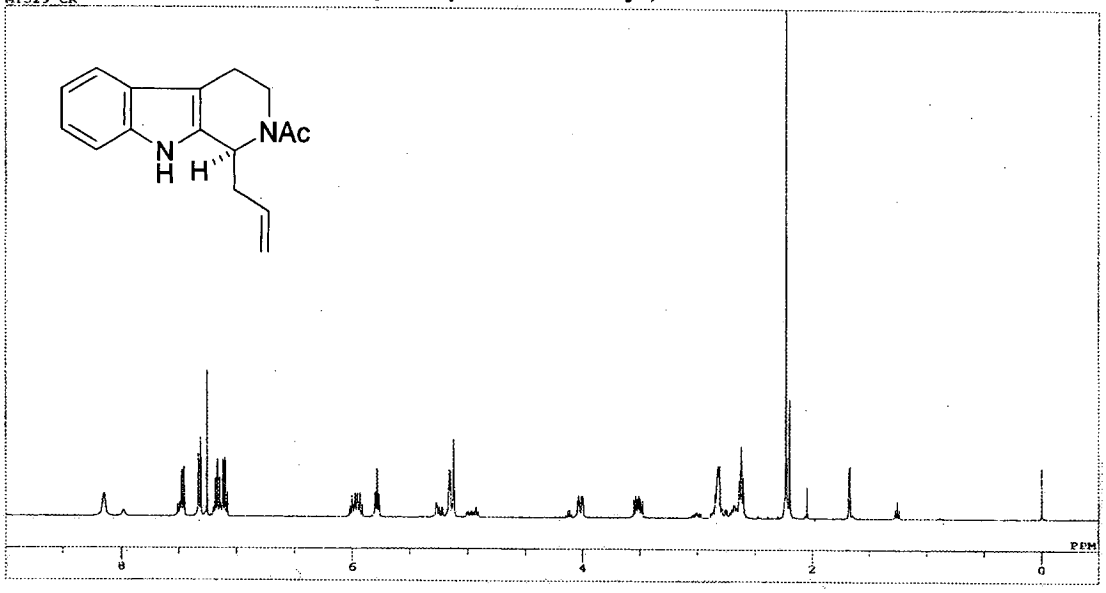
Tetrahedron*, **1993, *49*, 397-416, H. Waldmann *et al*



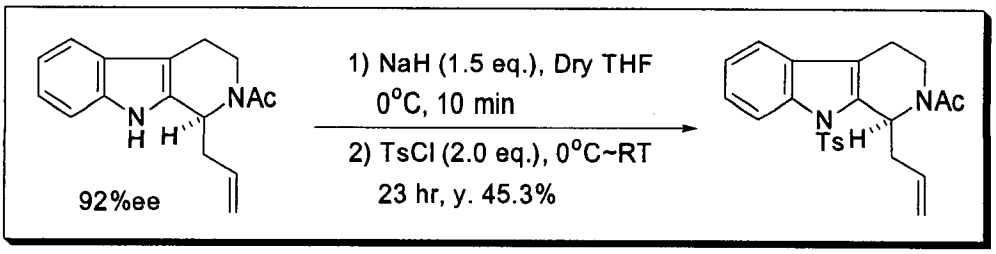
The allyl adduct (360.0 mg, 1.7 mmol) was dissolved in dry CH_2Cl_2 (7.0 ml), and Et_3N (710 μl, 5.1 mmol) and AcCl (242.0 μl, 3.4 mmol) were successively added to the solution at 0°C under Ar. After the reaction continued for another 2 h at room

temperature, sat.$NaHCO_3$ aqueous solution was added to the mixture. Then the mixture was extracted with CH_2Cl_2, and the organic layer thus obtained was dried over $MgSO_4$, and evaporated off. The residue was separated on NH-SiO_2 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

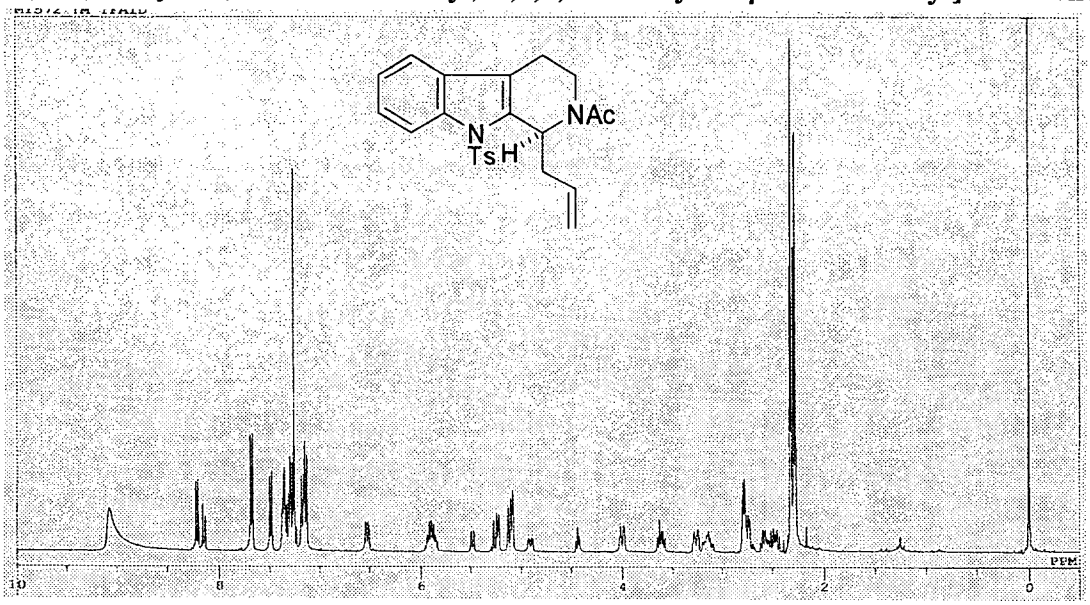


Pale yellow crystal. $[\alpha]^{23}_D$=+109.15 (c=1.07, MeOH), t_r(*R*)=14.5 min, t_r(*S*)=15.5 min, ee=92% (chiralcel OD, λ=254 nm, *i*PrOH/hexane=1/1); Anal. calcd for $C_{16}H_{18}N_2O$: C, 75.56; H, 7.13; N, 11.01. Found: C, 75.29; H, 7.31; N, 10.75. The product was obtained as a mixture of two conformational isomers (1:0.3). The NMR spectra of the major isomer are shown; ^{1}H-NMR (400 MHz, $CDCl_3$) δ3.23 (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); ^{13}C NMR (100 MHz, $CDCl_3$) 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.



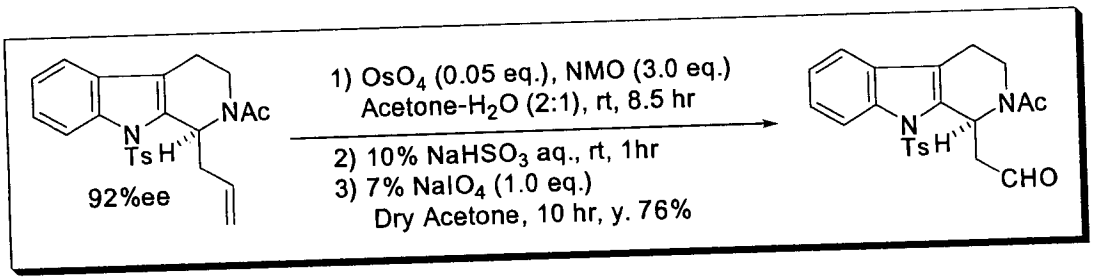
To the NaH (43.5 mg, 1.09 mmol) suspension in THF (13.0 ml) was added the starting material (184.0 mg, 724.4 μmol) under Ar at 0°C, then the mixture was allowed to react for 10 min. Then *p*-toluenesulfonyl chloride (276.2 mg, 1.45 mmol) was added, and the reaction was continued for 23 h. After the addition of 0.2 N HCl, the mixture was extracted with CH_2Cl_2, which was dried over $MgSO_4$ and evaporated off to leave a residue. The residue was chromatographed on silica gel (10% AcOEt in CH_2Cl_2) 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



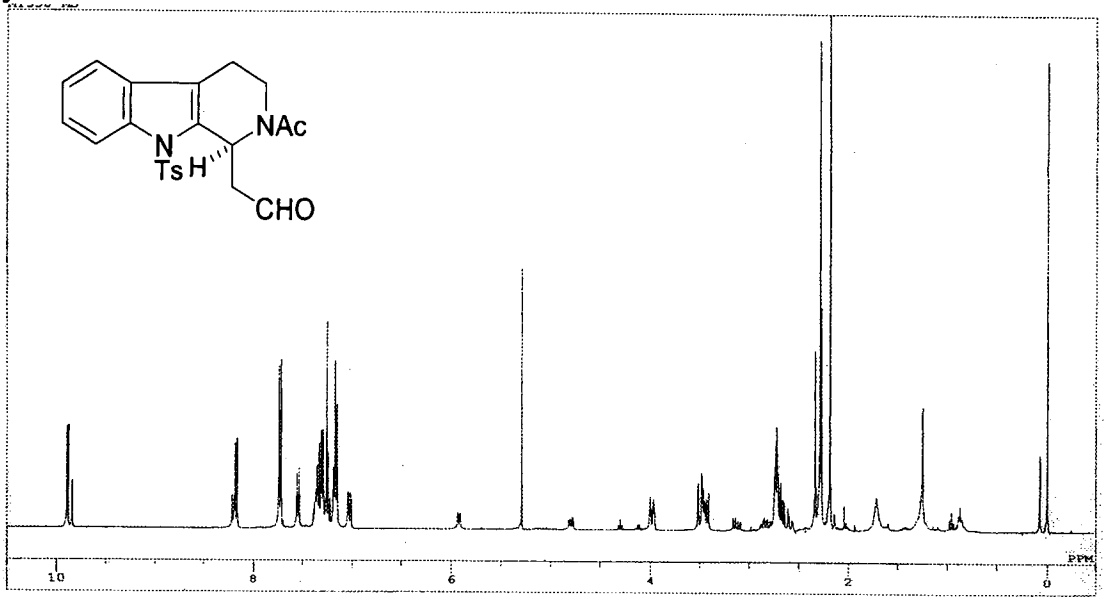
Slightly yellow amorphous. $[\alpha]^{23}_D$=+169.12 (c=0.97, MeOH), t_r(*S*)=17.5 min, t_r(*R*)=18.9 min, ee=92% (chiralcel OD, λ=254 nm, *i*PrOH/hexane=1/5); HRMS (FAB^+) *m/z*: Calcd for $C_{23}H_{25}N_2O_3S$ $(M+H)^+$ 409.1586, Found 409.1559; Since the product was obtained as a mixture of two conformational 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}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}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.

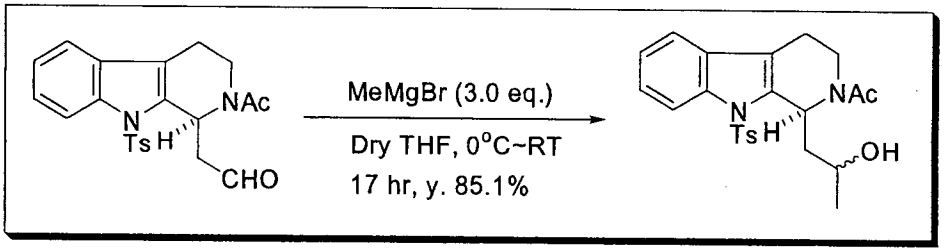


To the acetone (6.0 ml)/H_2O (12 ml) solution of N-methylmorpholine (50wt.% sol. in H_2O) (483.5 μl, 2.06 mmol) was added OsO_4 (4 wt.% sol. in H_2O) (218.5 μl, 34.4 μmol). Then the acetone solution (18 ml) of the starting material (280.6 mg, 687.7 μmol) was added, and the mixture was allowed to react 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



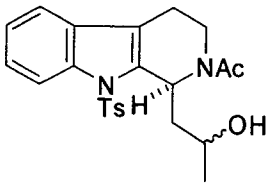
Slightly yellow amorphous. $[\alpha]^{23}_{D}$=+308.52 (c=0.87, $CHCl_3$); HRMS (FAB^+) *m/z*: Calcd for $C_{22}H_{23}N_2O_4S$ $(M+H)^+$ 411.1379, Found 411.1346; The product was obtained as a mixture of two conformational isomers (1:0.4). The NMR spectra of the major isomer are shown; ^{1}H-NMR (400 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.



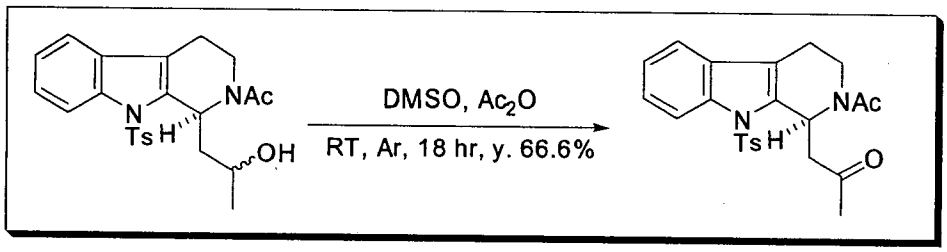
To the dry THF solution (6.0 ml) of the starting material was added MeMgBr (3.0 M sol. in Et_2O) (120.0 μl, 360.0 μmol) at 0°C under Ar, and the mixture was allowed to react

for 17 h under ambient temperature. After cooling to 0°C, saturated NH_4Cl aqueous solution was added, and the mixture was extracted with CH_2Cl_2. The organic layer was dried over $MgSO_4$, 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

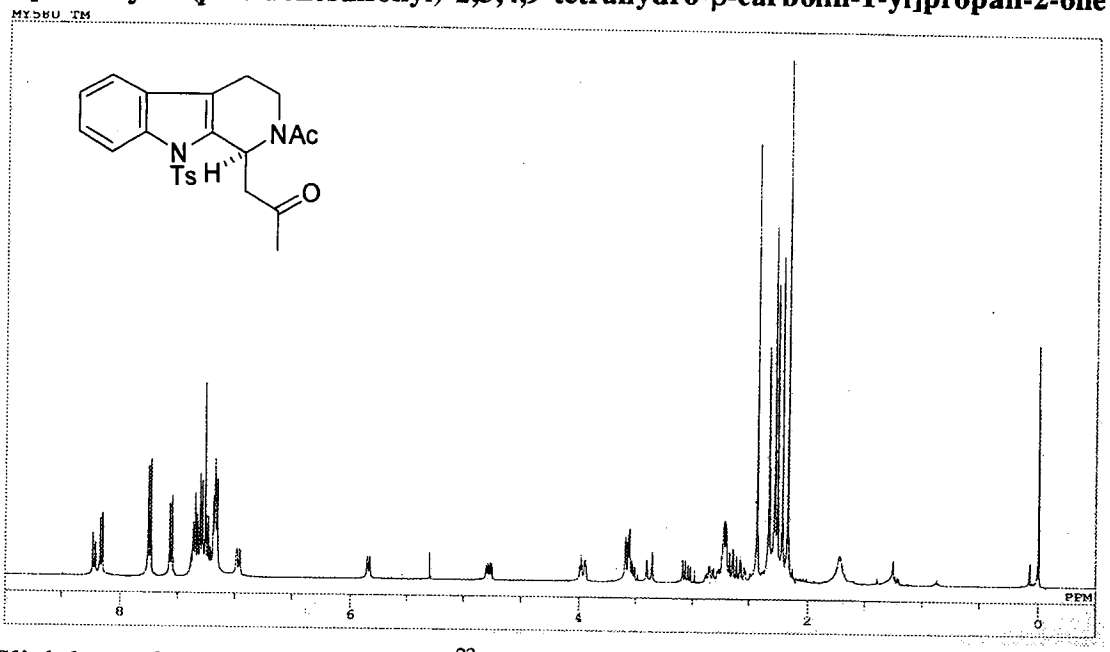


HRMS (FAB$^+$) *m/z*: Calcd for $C_{23}H_{27}N_2O_4S$ $(M+H)^+$ 427.1692, Found 427.1682

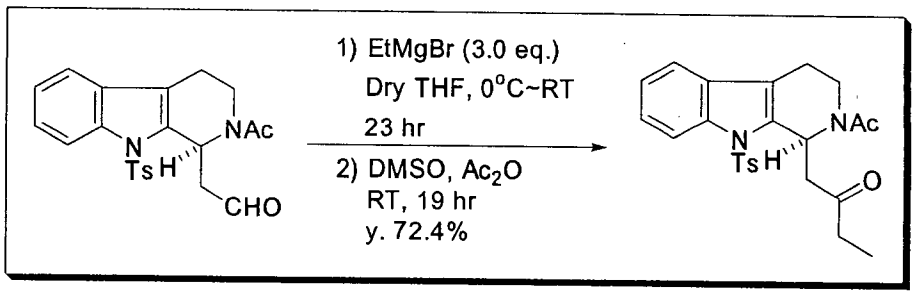


To the dry DMSO solution (1.0 ml) of the starting material (9.8 mg, 23.0 μmol) was added acetic anhydride (0.7 ml) under Ar at room temperature, and the mixture was allowed to react for 18 h. Then sat.$NaHCO_3$ aqueous solution was added, and the mixture was exdstracted with CH_2Cl_2. The organic layer thus formed was dried over $MgSO_4$, 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

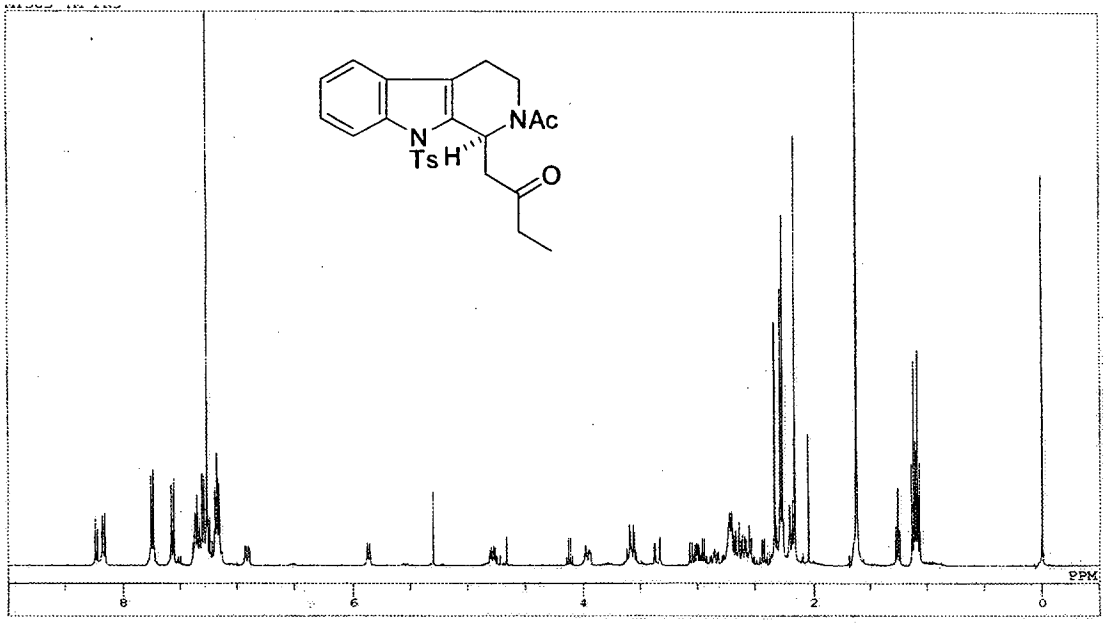


Slightly yellow amorphous. $[\alpha]^{23}_{D}$=+187.10 (c=1.05, MeOH), $t_r(S)$=16.7 min, $t_r(R)$=20.3 min, ee=89% (chiralcel OD, λ=254 nm, *i*PrOH/hexane=1/3); HRMS (FAB^+) *m/z*: Calcd for $C_{23}H_{25}N_2O_4S$ $(M+H)^+$ 425.1535, Found 425.1566; The product was obtained as a mixture of two conformational isomers (1:0.6). The NMR spectra of the major isomer are shown; ^{1}H-NMR (400 MHz, $CDCl_3$) 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); ^{13}C NMR (100 MHz, $CDCl_3$) 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



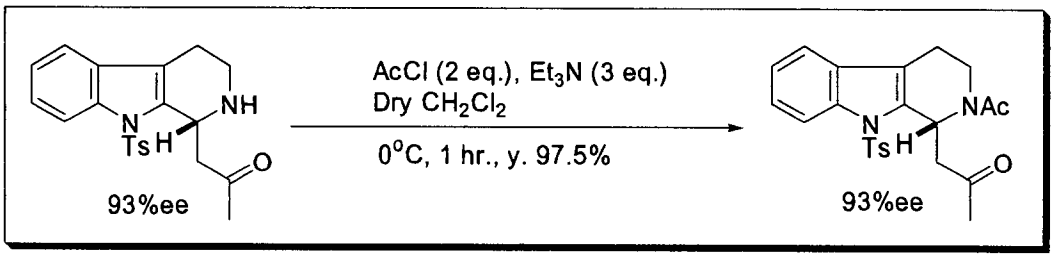
To the dry THF solution (5.0 ml) of the starting material (45.9 mg, 1120.0 μmol) was added EtMgBr (1.0 M sol. in THF) (335.9 μl, 335.9 μmol) at 0°C under Ar, and the mixture was allowed to react at ambient temperature for 23 h. After cooling, sat.NH_4Cl aqueous solution was added, and the mixture was extracted with CH_2Cl_2. 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.$NaHCO_3$ aqueous solution. The mixture thus obtained was extracted with CH_2Cl_2, and the organic layer was dried over $MgSO_4$, 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



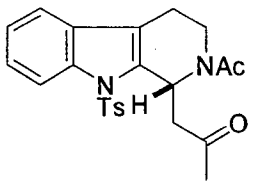
Slightly yellow amorphous. $[\alpha]^{23}_D$=194.90 (c=1.22, MeOH); t_r(*S*)=14.7 min, t_r(*R*)=16.2 min, ee=90% (chiralcel OD, λ=254 nm, *i*PrOH/hexane=1/2); HRMS (FAB^+) *m/z*: Calcd for $C_{24}H_{27}N_2O_4S$ $(M+H)^+$ 439.1692, Found 439.1701; The product was obtained as a mixture of two conformational isomers (1:0.6). The NMR spectra of the major isomer are shown; ^1H NMR (400 MHz, $CDCl_3$) 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.

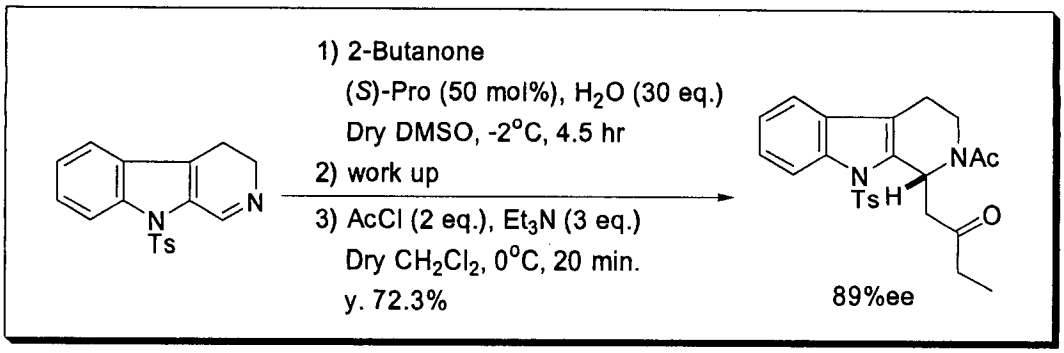


To the dry CH_2Cl_2 solution (2.0 ml) of the starting material were added Et_3N (21.0 μl, 152.4 μmol) and AcCl (7.2 μl, 101.6 μmol) successively at 0°C under Ar atmosphere, and the mixture was allowed to react for 1 h at room temperature. After the addition of water at 0°C, the mixture was extracted with CH_2Cl_2. The organic layer thus obtained was dried over $MgSO_4$, and evaporated off to leave a residue, which was chromatographed on silica gel (50% AcOEt in CH_2Cl_2) to give the product (21.0 mg, 97.5 %).

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

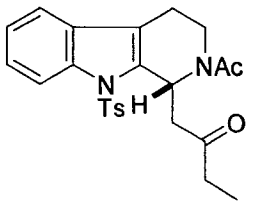


$[\alpha]^{23}_D$=-195.52 (c=1.05, MeOH), t_r(*S*)=16.7 min, t_r(*R*)=20.3 min, ee=93% (chiralcel OD, λ=254 nm, *i*PrOH/hexane=1/3)



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 H_2O (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.$NaHCO_3$ aqueous solution, the mixture was extracted with CH_2Cl_2. The organic layer was washed with H_2O, dried over $MgSO_4$, and evaporated off. The residue thus obtained was dissolved in dry CH_2Cl_2 (2.0 ml), then Et_3N (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 H_2O at 0°C. The mixture was extracted with CH_2Cl_2, which was dried over $MgSO_4$, 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. $[\alpha]^{23}_D$=-189.52 (c=0.91, MeOH); t_r(*S*)=14.3 min, t_r(*R*)= 16.2 min, ee=89% (chiralcel OD, λ=254 nm, *i*PrOH/hexanes=1/2)