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Diastereoselective Pinacol Coupling Reactions of α-Ketoamides Mediated by SmI_2 : Synthesis of Enantiomerically Pure both *S* and *R* Quaternary Tartaric acids.

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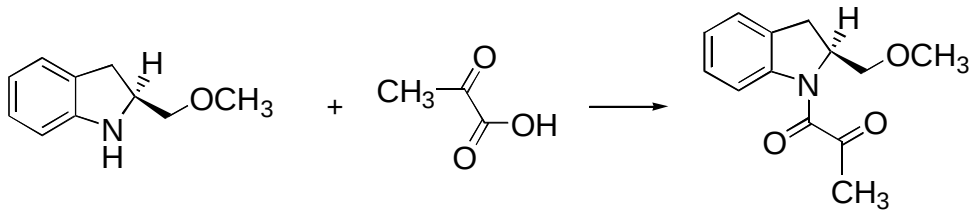
Supporting Information for:

General. All dry solvents were freshly distilled under nitrogen from the appropriate drying agent before use. Methylene chloride was distilled over calcium hydride and tetrahydrofuran was distilled over sodium-benzophenone. Oxygen- and /or moisture-sensitive reactions were carried out in well-dried glassware equipped with tight-fitting rubber septa and under a possive pressure of dry helium. Reagents and solvents were handled by using standard syringe techniques. Analytical thin layer chromatography (TLC) was performed on precoated silica gel glass plate (layer thickness : 0.25 mm, 60 F-254, E. Merck). Visualization was accomplished with UV light (254 nm), typical TLC indicating solution (p-anisaldehyde/sulfuric acid/ethanol/acetic acid), iodine, and/or phosphomolibdic acid solution. Flash column chromatography was performed by the method of Still (using E. Merck 230 –400 mesh ASTM silica gel). Proton nuclear magnetic resonance spectroscopy (^{1}H NMR) were recorded on Bruker Fourier Transform AC 200 (200 MHz) and Bruker Fourier Transform AM 300 (300 MHz) spectrometers. Chemical Shifts were reported in unit, parts per million (ppm) relative to the singlet as 7.24 ppm for chloroform-d. Splitting patterns were designated as s (singlet), d (doublet), t (triplet), dt (doublet of triplets), q (quartet), m (multiplet) and br (broadened). Coupling constants (J value) was reported in Hertz unit (Hz). Carbon-13 nuclear magnetic resonance spectroscopy (^{13}C NMR) were recorded on Bruker Fourier Transform AC 200 (50 MHz) and Bruker Fourier Transform AM 300 (75 MHz) spectrometers, and were fully decoupled by broad-band decoupling. Chemical shifts were reported in ppm with the center line of the triplet for chloroform-d set at 77.00. High resolution mass spectra were obtained on a Jeol JMS-SX-102.

1. Preparation of α-ketoamides and the characterization data

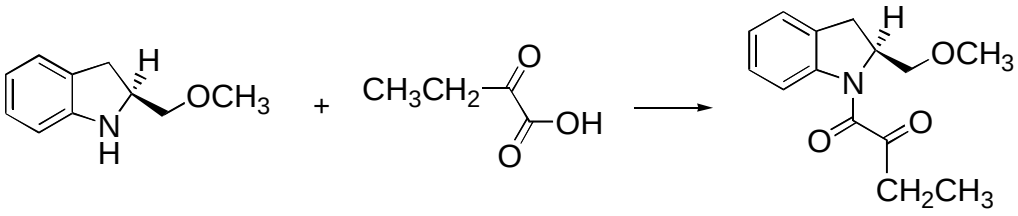
(1). Synthesis of (*S*)-*N*-pyruvoyl-2-(methoxymethyl)indoline



1a

To a methylene chloride (25 ml) solution of (*S*)-2-methoxymethyl-indoline(300 mg, 1.184 mmol)which was prepared from commercially available (*S*)-(–)-indoline-2-carboxylic acid(Aldrich Co.), pyruvic acid (186 mg, 2.11 mmol) and DCC (436 mg, 2.12 mmol) was added at room temperature. After the mixture was stirred at room temperature for 20h, the resulting precipitate was filtered. The filtrate was washed with 1N HCl, satd. aq. $NaHCO_3$ and water. The organic layer dried over $MgSO_4$, filtered and condensed under the reduced pressure. The residue was chromatographed on silica gel column (CH_2Cl_2) to give (*S*)-*N*-pyruvoyl-2-(methoxymethyl)-indoline (185 mg, 67 %). $[\alpha]_D^{23}$ = –22.4 (c = 1.13, CH_2Cl_2); ^{1}H NMR ($CDCl_3$) δ 2.45 (s, 3H), 2.62 (d, 1H), 3.2 ~ 3.4 (m, 2H), 3.28 (s, 3H), 3.40 (m, 1H), 5.18 (m, 1H), 7.07 (m, 1H), 7.26 (m, 2H), 8.23 (d, 1H) ; ^{13}C NMR ($CDCl_3$) δ 26.52, 31.07, 57.59, 58.62, 116.08, 124.81, 124.92, 127.80, 130,64, 141.32, 164.81, 196.56 ; MS m/z (%) 233.1056 (M^+, 100), 190 (49.6), 188 (31.5), 132 (36.2), 118 (49.1).

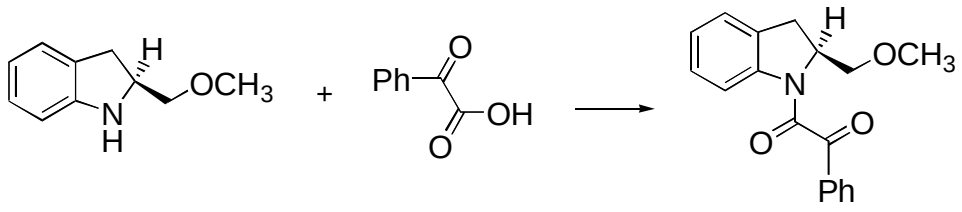
(2) Synthesis of (*S*)-*N*-(2-oxobutanoyl)-2-(methoxymethyl)indoline



1b

(*S*)-*N*-(2-Oxobutanoyl)-2-(methoxymethyl)indoline was prepared from (*S*)-2-methoxymethylindoline and 2-ketobutyric acid in 82 % by the same method used in the preparation of (*S*)-*N*-pyruvoyl-2-(methoxymethyl)indoline. $[\alpha]_D^{17}$ = –46.3 (c = 1.01, CH_2Cl_2); ^{1}H NMR ($CDCl_3$) δ 1.07 (t, 3H), 2.56 (m, 2H), 3.05 (m, 1H), 3.18 (s, 3H), 3.16 ~ 3.22 (m, 2H), 3.32 (m, 1H), 5.08 (m, 1H), 7.0 (m, 1H), 7.17 (m, 2H), 8.16 (d, 1H) ; ^{13}C NMR ($CDCl_3$) δ 7.09, 31.17, 32.08, 57.60, 58.70, 74.58, 118.16, 124.80, 124.92, 127.78, 130,72, 141.38, 165.09, 199.86 ; MS m/z (%) 247.1204 (M^+, 100), 190 (35.2), 132 (28.2), 118 (55.5).

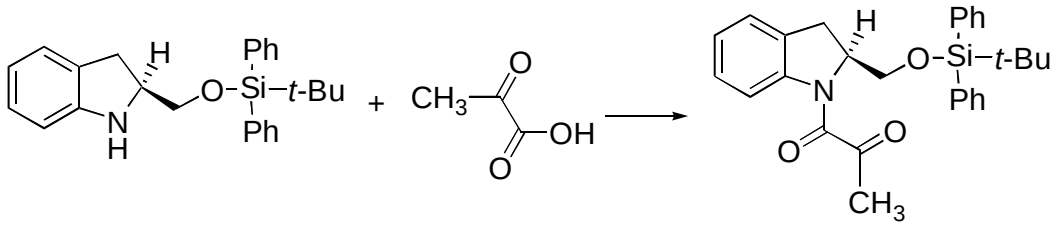
(3) Synthesis of (*S*)-*N*-benzoylformyl-2-(methoxymethyl)indoline



1c

To a THF (25 ml) solution of (*S*)-2-methoxymethylindoline (300 mg, 1.84 mmol), benzoylformic acid (316 mg, 2.11 mmol) and DCC (436 mg, 2.12 mmol) was added at room temperature. After the mixture was stirred at room temperature for 20 h, the resulting precipitate was filtered. The filtrate was washed with 1N HCl, satd. aq. $NaHCO_3$ and water. The organic layer dried over $MgSO_4$, filtered and condensed under the reduced pressure. The residue was chromatographed on silica gel column (CH_2Cl_2) to give (*S*)-*N*-benzoylformyl-2-(methoxymethyl)indoline (397 mg, 73 %) : $[\alpha]_D^{24}$ = -187 (c = 1.06, CH_2Cl_2); ^{1}H NMR ($CDCl_3$) δ 2.74 (d, 1H), 2.86 (s, 3H), 3.2 ~ 3.5 (m, 3H), 5.01 (m, 1H), 7.0 ~ 7.3 (m, 3H), 7.4 ~ 7.6 (m, 3H), 8.08 (d, 2H), 8.33 (d, 1H) ; ^{13}C NMR ($CDCl_3$) δ 31.43, 31.61, 60.26, 62.27, 64.91, 118.2, 124.9, 127.7, 128.4, 130,2, 130.8, 133.7, 133.9, 141.4, 164.5, 168.3, 164.63, 189.03, 190.46 ; MS m/z (%) 295 (M^+, 3.9), 222 (3.8), 190 (15.4), 132 (29.2), 105 (100), 77 (29.7).

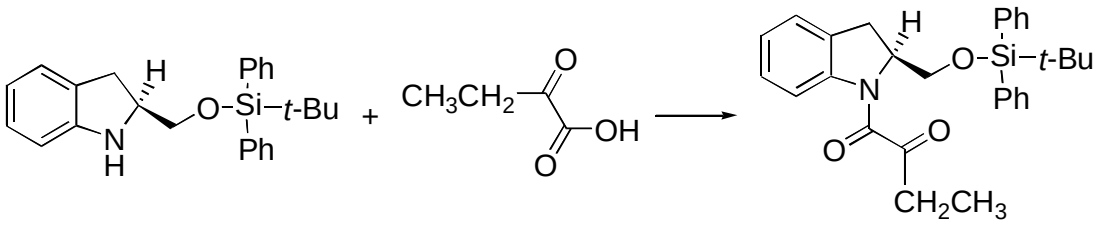
(4) Synthesis of (*S*)-*N*-pyruvoyl-2-(*t*butyldiphenylsilyloxymethyl)indoline



1d

(*S*)-*N*-Pyruvoyl-2-(*t*butyldiphenylsilyloxymethyl)indoline was prepared from (*S*)-2-*t*butyldiphenylsiloxymethylindoline and pyruvic acid in 80 % by the same method used in the preparation of (*S*)-*N*-pyruvoyl-2-(methoxymethyl)-indoline : $[\alpha]_D^{25}$ = –40.3 (c = 0.67, CH_2Cl_2); ^{1}H NMR ($CDCl_3$) δ 0.95 (s, 9H), 2.48 (s, 3H), 3.0 ~ 3.37 (m, 2H), 3.62 ~ 3.79 (m, 2H), 5.13 (m, 1H), 7.08 ~ 7.62 (m, 13H), 8.27 (d, J= 7.75, 1H) ; ^{13}C NMR ($CDCl_3$) δ 19.01, 26.58, 27.01, 31.07, 59.88, 66.51, 117.93, 124.56, 124.9, 127.04, 127.60, 129.72, 131.72, 132.86, 135.34, 142.12, 162.43, 197.15 ; IR (NaCl) 1718.6, 1645.5, 1598.3, 1462.5, 1427.0, 1112.8 cm^{-1} ; MS m/z (%) 457.2046 (M^+, 15.0), 400 (100), 328 (11.4), 252 (17.9), 312 (12.9), 199 (43.1), 183 (21.5), 135 (39.8), 130 (27.4), 118 (40.1).

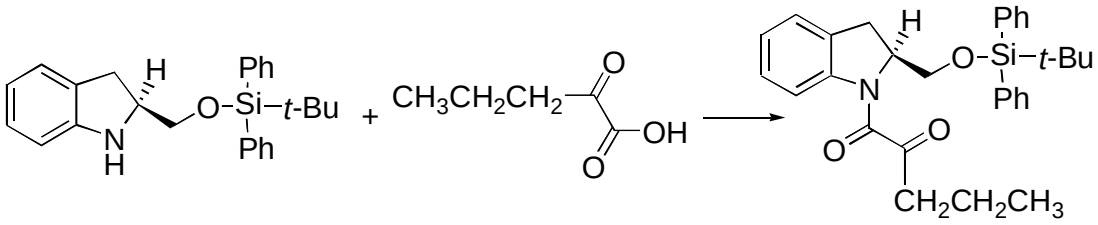
(5) Synthesis of (*S*)-*N*-(2-oxobutanoyl)-2-(*t*butyldiphenylsilyloxymethyl)-indoline



1e

(*S*)-*N*-(2-oxobutanoyl)-2-(*t*butyldiphenylsilyloxymethyl)indoline was prepared from (*S*)-2-*t*butyldiphenylsilyloxymethylindoline and 2-ketobutyric acid in 70 % by the same method used in the preparation of (*S*)-*N*-pyruvoyl-2-(methoxymethyl)indoline ; $[\alpha]_D^{25}$ = –40 (c = 0.8, CH_2Cl_2) ; ^{1}H NMR($CDCl_3$) δ 0.94 ~ 1.03 (m, 12H), 2.55 (m, 1H), 2.95 (m, 1H), 3.12 ~ 3.37 (m, 2H), 3.65 ~ 3.82 (m, 2H), 5.06 (m, 1H), 7.08 ~ 7.62 (m, 13H), 8.27 (d, J= 7.65, 1H) ; ^{13}C NMR ($CDCl_3$) δ 6.99, 19.10, 26.62, 31.82, 32.65, 60.01, 66.58, 77.33, 118.04, 124.67, 125.08, 127.29, 127.76, 129.79, 131.87, 132.91, 135.46, 142.27, 163.08, 200.39 ; IR (NaCl) 1715.3, 1648.0, 1598.2, 1483.1, 1113.4 cm^{-1} ; MS m/z (%) 471.2240 (M^+, 7.0), 414 (100), 336 (20), 330 (11.7), 328 (16.3), 298 (6.0), 252 (13.5), 199 (5.6), 57 (5.2).

(6) Synthesis of (*S*)-*N*-(2-oxopentanoyl)-2-(*t*butyldiphenylsilyloxymethyl)-indoline

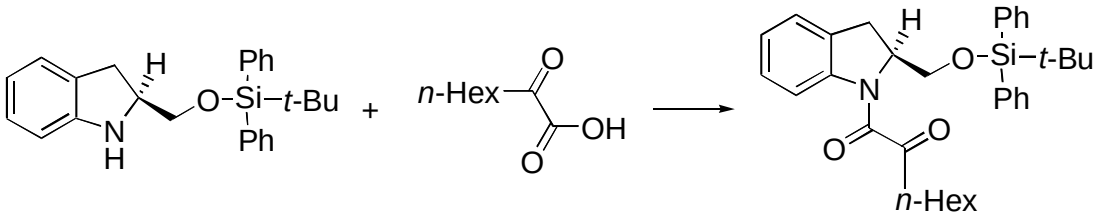


1f

$[\alpha]_D^{25}$ = –41.3 (c = 1.67, CH_2Cl_2) ; ^{1}H NMR($CDCl_3$) δ 0.82 ~ 0.90 (m, 12H), 1.45 ~ 1.54 (m, 2H), 2.40 ~ 2.53 (m, 1H), 2.80 ~ 2.92 (m, 1H), 3.16 (d, 1H), 3.32 ~ 3.48 (m, 1H), 3.54 ~ 3.78 (m, 2H), 5.00 (m, 1H), 7.07 ~ 7.58 (m, 13H), 8.22 (d, J= 7.6, 1H) ; ^{13}C NMR ($CDCl_3$) δ 13.45, 16.48, 26.55, 31.76, 41.07, 59.95, 66.58, 117.94, 124.57, 124.99, 127.21, 127.69, 129.72, 131.81, 132.88, 135.40, 142.28, 163.06, 199.69 ; IR (NaCl) 1713.0, 1646.8, 1598.2, 1483.0, 1113.2 cm^{-1} ; MS m/z (%) 485.2340 (M^+, 15.0), 429 (34.4), 428 (100), 350 (5.8), 328 (6.2), 252 (13.0).

(7) Synthesis of (*S*)-*N*-(2-oxohexanoyl)-2-

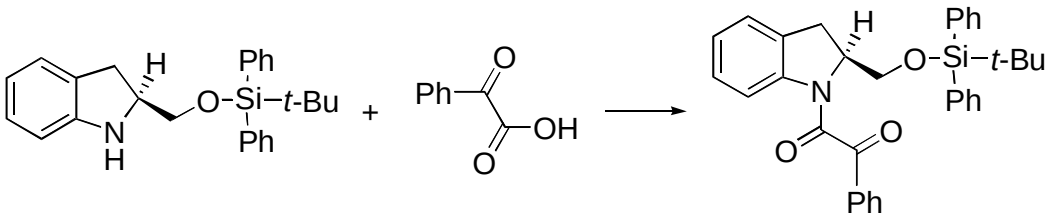
(*t*butyldiphenylsilyloxymethyl)-indoline



1g

$[\alpha]_D^{25}$ = -40.7 (c = 1.67, CH_2Cl_2) ; ^{1}H NMR($CDCl_3$) δ 0.87 ~ 0.99 (m, 12H), 1.23 ~ 1.32 (m, 6H), 1.43 ~ 1.56 (m, 2H), 2.41 ~ 2.58 (m, 1H), 2.85 ~ 3.02 (m, 1H), 3.18 (d, 1H), 3.33 ~ 3.45 (m, 1H), 3.61 ~ 3.82 (m, 2H), 5.04 (m, 1H), 7.11 ~ 7.61 (m, 13H), 8.26 (d, J= 7.7, 1H) ; ^{13}C NMR ($CDCl_3$) δ 13.93, 18.99, 22.35, 22.90, 26.51, 28.55, 30.45, 31.39, 31.70, 39.21, 39.94, 59.90, 66.57, 117.90, 124.53, 124.95, 127.17, 127.68, 129.69, 131.78, 132.81, 135.36, 142.26, 163.03, 199.81 ; IR (NaCl) 1714.1, 1647.0, 1598.1, 1482.6, 1113.1 cm^{-1} ; MS m/z (%) 527.2889 (M^+, 11.0), 470 (100), 392 (12.5), 328 (12.1), 252 (19.0), 213 (8.1), 199 (16.5), 183 (11.1), 135 (21.7), 118 (19.3), 85 (5.1), 57 (8.1).

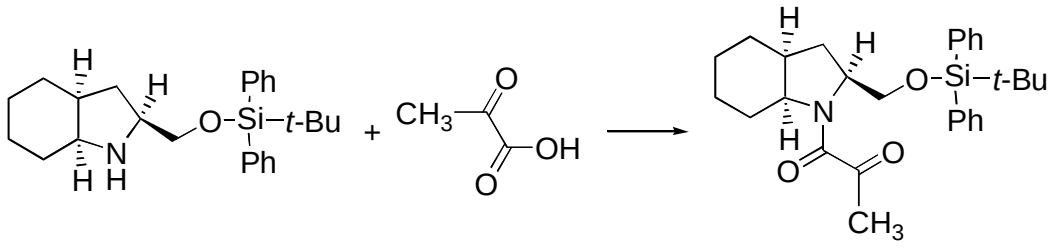
(8) Synthesis of (*S*)-*N*-benzoylformyl-2-(*t*butyldiphenylsilyloxymethyl)-indoline



1h

$[\alpha]_D^{25}$ = -59.8 (c = 4.53, CH_2Cl_2) ; ^{1}H NMR($CDCl_3$) δ 0.91 (s, 9H), 3.09 ~ 3.43 (m, 2H), 3.69 ~ 3.72 (m, 2H), 4.23 (m, 1H), 7.27 ~ 7.98 (m, 18H), 3.39 (d, 1H) ; ^{13}C NMR ($CDCl_3$) δ 18.91, 26.45, 31.77, 60.09, 65.99, 113.10, 117.60, 127.50, 124.68, 125.10, 127.57, 128.75, 129.77, 129.94, 131.56, 132.76, 133.07, 134.67, 135.40, 141.89, 164.04, 188.98. IR (NaCl) 1692.5, 1680.9, 1648.4, 1597.0, 1485.4, 1113.9 cm^{-1}.

(9) Synthesis of (2*S*, 3a*S*, 7a*S*)-*N*-pyruvoyl-2-(*t*butyldiphenylsilyloxy-methyl)indoline

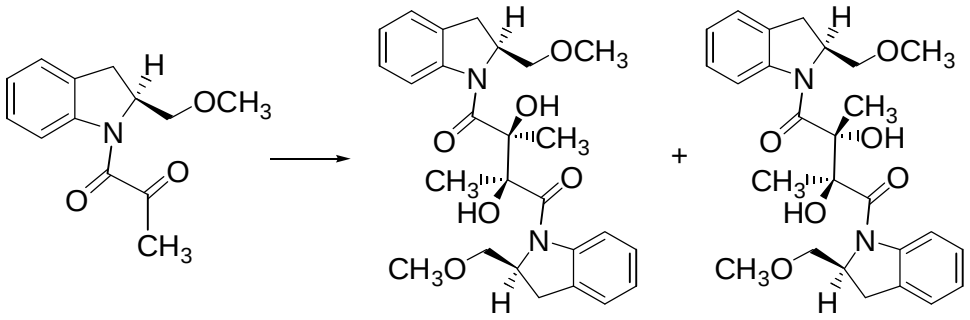


1a'

$[\alpha]_D^{25}$ = -30.2 (c = 1.67, CH_2Cl_2) ; ^{1}H NMR($CDCl_3$) δ 0.93 (s, 9H), 1.05 ~ 1.27 (m, 4H), 1.48 ~ 1.64 (m, 5H), 1.72 ~ 1.86 (m, 3H), 2.10 ~ 2.22 (m, 1H), 2.38 (s, 3H), 3.79 ~ 3.94 (m, 1H), 4.12 (m, 1H), 7.32 ~ 7.67 (m, 10H) ; ^{13}C NMR ($CDCl_3$) δ 19.21, 19.93, 23.77, 25.76, 26.84, 27.23, 27.92, 28.48, 37.06, 58.81, 59.21, 63.02, 127.60, 129.57, 133.28, 135.50, 164.55, 198.30 ; IR (NaCl) 1631.9, 1620.8, 1605.4, 1471.8, 1459.4, 1112.5 cm^{-1} ; MS m/z (%) 463.2540 (M^+, 25.8), 420 (68.8), 406 (100), 378 (60.3), 362 (15.5), 334 (78.9), 314 (26.2), 292 (34.6), 268 (66.4), 240 (32.4), 199 (82.1), 183 (56.2), 162 (37.9), 139 (47.8), 124 (79.4), 95 (37.8), 81 (67.5).

2. Asymmetric pinacol coupling reaction of (*S*)-*N*-pyruvoyl-2-(methoxy-methyl)indoline

A THF (6.7 ml) solution of SmI_2 (0.1M in THF solution) was added dropwise to a THF (4 ml) solution of (*S*)-*N*-pyruvoyl-2-(methoxymethyl)indoline (78.1 mg, 0.335 mmol), HMPA (233 μl, 1.34 mmol) and *t*BuOH (126 μl, 1.34 mmol) at –78 ^{o}C. After stirring at –78 ^{o}C for 10 min., the mixture was quenched with 1N HCl solution and extracted with CH_2Cl_2. The organic layer was dried over $MgSO_4$ and condensed under the reduced pressure. The reaction mixture was roughly purified by flash column chromatography on silica gel (EtOAc : CH_2Cl_2 : n-hexane = 1 : 4 : 5 (v/v/v) to afford the coupled product (32.9 mg, 42 %, (*S,S*) : (*S,R*) = 95 : 5). The diastereomers of **2a** and **4a** were readily separated by flash column chromatography. Diastereomeric ratio of (*S,S*)-diastereomer (**2a**) and (*S,R*)-diastereomer (**4a**) was determined by HPLC analysis.



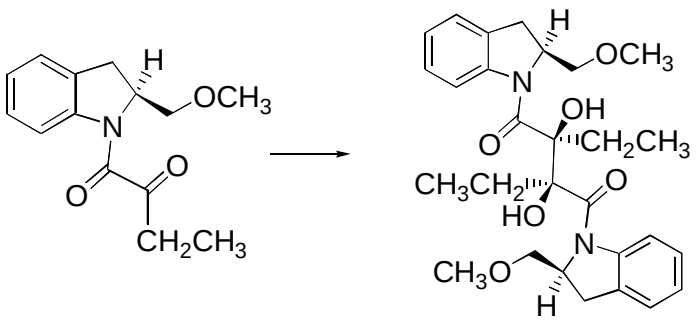
1a **2a** **4a**

(*S,S*)-diastereomer (**2a**) ; $[\alpha]_D^{18}$ = +3.08 (c= 0.778, CH_2Cl_2) ; ^1H NMR ($CDCl_3$) δ 1.53 (s, 6H), 2.96 (d, 2H), 3.1 ~ 3.3 (m, 4H), 3.32 (s, 6H), 3.62 (m, 2H), 5.35 (m, 2H), 6.09 (s, 2H), 7.0 ~ 7.2 (m, 6H), 7.88 (d, 2H) ; ^{13}C NMR ($CDCl_3$) δ 20.12, 32.43, 59.14, 59.58, 73.67, 80.45, 119.64, 124.96, 125.21, 126.92, 131.53, 142.83, 177.95 ; IR (NaCl) 3350 (br), 1620.9, 1590.1, 1478.3, 1265.0, 1121.3 cm^{-1} ; MS m/z (%) 468.2221 (M^+, 84), 306 (48.3), 278 (95.8), 260 (9.4), 235 (24.7), 190 (20.5), 164 (55.1), 163 (13.8), 132 (26.6), 118 (100), 97 (11.6).

(*S,R*)-diastereomer (**4a**) ; ^1H NMR ($CDCl_3$) δ 1.55 (s, 3H), 1.74 (s, 3H), 2.95 (d, 2H), 3.0 ~ 3.3 (m, 4H), 3.28 (s, 3H), 3.30 (s, 3H), 3.60 (m, 1H), 3.72 (m, 1H), 5.35 (m, 1H), 5.87 (m, 1H), 6.27 (s, 1H), 6.87 (s, 1H), 7.0 – 7.2 (m, 6H), 7.91 (d, 1H), 8.04 (d, 1H) ; ^{13}C NMR ($CDCl_3$) δ 23.9, 25.6, 32.3, 58.9, 59.0, 59.4, 59.9, 73.8, 74.2, 79.5, 81.7, 119.9, 124.9, 125.0, 125.1, 125.2, 126.7, 131.5, 131.8, 142.8, 151.3, 175.2, 175.3.

3. Asymmetric pinacol product of (*S*)-*N*-(2-oxobutanoyl)-2-(methoxy-methyl)indoline

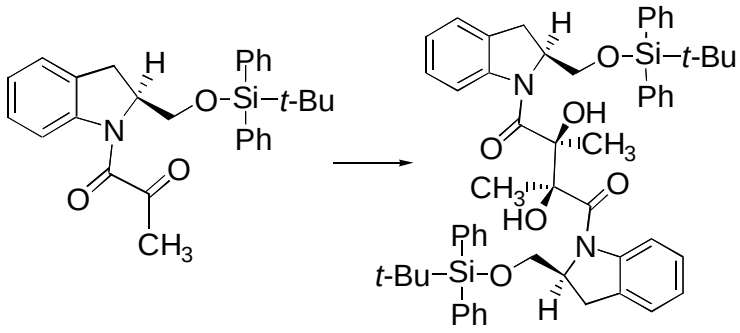
The coupling reaction was carried out under the same conditiom as the procedure mentioned pinacol coupling reaction of (*S*)-*N*-pyruvoyl-2-(methoxymethyl)indoline (39 %). Diastereomeric ratio of (*S,S*) and (*S,R*) stereoisomers was determined by HPLC analysis ((*S,S*) : (*S,R*) = 98 : 2).



1b **2b**

(*S,S*)-diastereomer (**2b**) : $[\ ]_D^{16}$ = –52.8 (c = 0.835, CH_2Cl_2) ; ^1H NMR ($CDCl_3$) δ 1.04 (t, 6H), 1.90 (m, 2H), 2.18 (m, 2H), 3.02 (d, 2H), 3.18 (m, 2H), 3.29 (m, 2H), 3.39 (s, 6H), 3.77 (m, 2H), 5.71 (m, 2H), 6.63 (s, 2H), 7.0 ~ 7.3 (m, 6H), 7.81 (d, 2H) ; ^{13}C NMR ($CDCl_3$) δ 8.64, 27.29, 32.64, 59.04, 59.36, 73.37, 84.53, 119.91, 125.12, 125.24, 126.62, 131.64, 142.75, 177.52 ; IR (NaCl) 3320 (br), 1615.7, 1584.7, 1478.0, 1388.3, 1270.3, 1122.8 cm^{-1} ; MS m/z (%) 496.2545 (M^+, < 0.1), 279 (3.4), 249 (2.1), 164 (16.3), 118 (60.1), 71 (10.1), 57 (100).

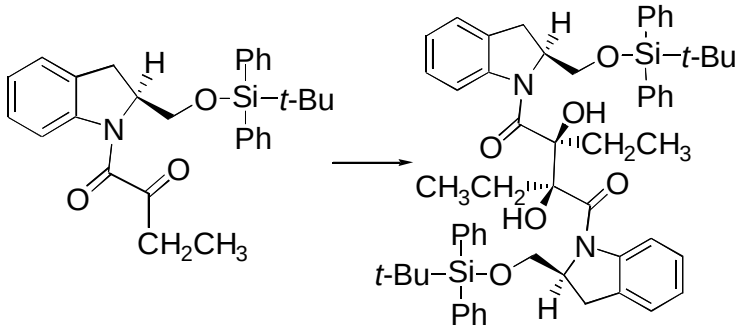
4. Asymmetric pinacol product of (*S*)-*N*-pyruvoyl-2-(*t*butyldiphenyl-silyloxymethyl)indoline



1d **2d**

$[\alpha]_D^{25}$ = +39.2 (c = 1.0, $CHCl_3$) ; (*S,S*)-diastereomer (**2d**) ; ^1H NMR ($CDCl_3$) δ 0.96 (s, 9H), 1.51 (s, 3H), 3.20 (m, 2H), 3.66 ~ 3.94 (m, 2H), 5.36 (m, 1H), 5.96 (s, 1H), 7.03 ~ 7.59 (m, 13H), 7.78 (d, J= 8.3, 1H) ^{13}C NMR ($CDCl_3$) δ 19.18, 20.10, 26.73, 32.09, 61.45, 65.88, 80.29, 119.55, 124.62, 126.58, 127.60, 127.65, 129.56, 131.82, 133.26, 135.54, 143.30, 177.90 ; IR (NaCl) 3400 (br), 1260.6, 1590.1, 1478.1, 1394.8, 1111.9 cm^{-1} ; MS m/z (%) 916.4297 (M^+, < 0.1), 912 (74.0), 855 (6.8), 526 (17.1), 502 (25.3), 424 (22.7),402 (86.7), 400 (100), 330 (75.0), 328 (35.2), 296 (31.3), 252 (58.7), 213 (30.2), 199 (79.2), 118 (80.2).

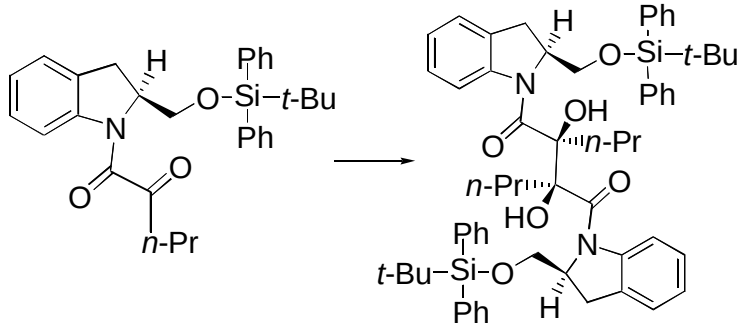
5. Asymmetric pinacol product of (*S*)-*N*-(2-oxobutanoyl)-2-(*t*butyldiphenyl-silyloxymethyl)indoline



1e **2e**

$[\alpha]_D^{25}$ = +37.6 (c = 1.0, $CHCl_3$) ; (*S,S*)-diastereomer (**2e**) ; ^{1}H NMR ($CDCl_3$) δ 0.85 (*t*, 3H), 1.03 (s, 9H), 1.80 ~ 2.09 (m, 2H), 3.13 ~ 3.15 (m, 2H), 3.45 ~ 3.55 (m, 1H), 4.08 ~ 4.15 (m, 1H), 5.71 (m, 1H), 6.53 (s, 1H), 6.92 ~ 7.65 (m, 14H) ; ^{13}C NMR ($CDCl_3$) δ 8.45, 19.21, 26.84, 27.43, 31.92, 61.29, 64.83, 84.12, 119.82, 124.79, 126.54, 127.67, 129.58, 131.59, 133.25, 135.53, 143.03, 177.22 ; IR (NaCl) 3350 (br), 1615.4, 1586.0, 1476.8, 1391.5, 1112.2 cm^{-1} ; MS m/z (%) 942.4737 (M^+, 9.0), 771, 743, 654, 559, 532, 475, 456, 430 (43.9), 396 (58.4), 366 (63.3), 327 (44.1), 300 (86.9), 280 (53.8), 239 (48.0), 212 (100), 151 (84.2), 115 (89.7).

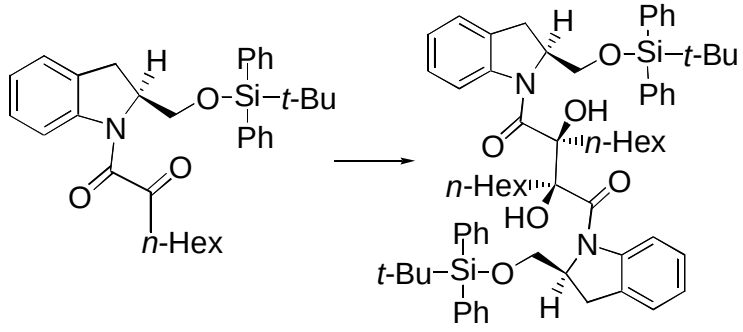
6. Asymmetric pinacol product of (*S*)-*N*-(2-oxopentanoyl)-2-(*t*butyldiphenyl-silyloxymethyl)indoline



1f **2f**

$[\alpha]_D^{25}$ = +21.7 (c = 1.0, $CHCl_3$) ; (*S,S*)-diastereomer (**2f**) ; ^{1}H NMR ($CDCl_3$) δ 0.85 ~ 0.97 (m, 5H), 1.02 (s, 9H), 1.72 ~ 2.10 (m, 2H), 3.12 (d, 2H), 3.46 ~ 3.51 (m, 1H), 4.09 ~ 4.12 (m, 1H), 5.67 (m, 1H), 6.51 (s, 1H), 6.97 ~ 7.63 (m, 14H) ; ^{13}C NMR ($CDCl_3$) δ 14.57, 17.18, 19.29, 26.89, 32.00, 36.86, 61.16, 64.86, 83.84, 119.90, 124.73, 124.83, 127.57, 129.63, 131.67, 133.39, 133.55, 135.58, 143.06, 177.37 ; IR (NaCl) 3390 (br), 1615.3, 1585.5, 1477.3, 1391.7, 1273.3, 1112.4 cm^{-1} ; MS m/z (%) 972.5030 (M^+, 62), 428 (100), 350 (37.67), 330 (79.38), 324 (35.38), 252 (68.23), 222 (20.59), 199 (79.04), 135 (65.40), 118 (88.38), 71 (55.85)

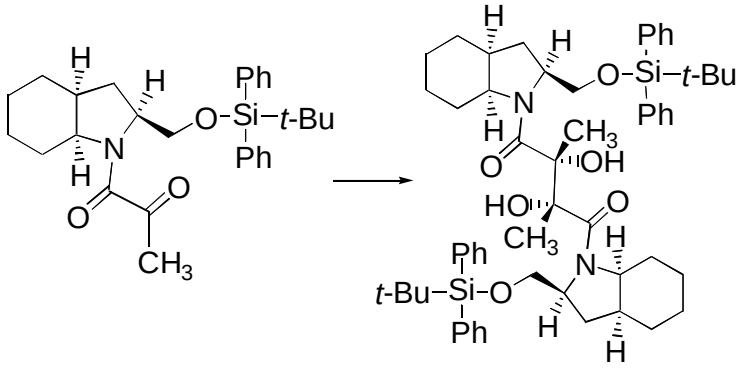
7. Asymmetric pinacol product of (*S*)-*N*-(2-oxohexanoyl)-2-(*t*butyldiphenyl-silyloxymethyl) indoline



1g **2g**

$[\alpha]_D^{25}$ = +22.5 (c = 1.1, $CHCl_3$) ; (*S,S*)-diastereomer (**2g**) ; ^{1}H NMR ($CDCl_3$) δ 0.83 ~ 0.87 (m, 12H), 1.23 ~ 1.55 (m, 6H), 2.09 ~ 2.12 (m, 2H), 3.12 ~ 3.35 (m, 2H), 3.58 ~ 3.71 (m, 2H), 4.81 (m, 1H), 6.29 (s, 1H), 6.92 ~ 7.53 (m, 13H), 8.18 (d, 1H). ^{13}C NMR ($CDCl_3$) δ 13.75, 13.95, 19.09, 22.02, 22.28, 26.59, 29.70, 31.76, 32.61, 60.06, 66.28, 83.50, 117.81, 124.74, 125.03, 126.84, 127.32, 127.73, 129.73, 131.69, 133.05, 135.57, 143.05, 164.01 ; IR (NaCl) 3450 (br), 1645.2, 1598.3, 1482.9, 1427.1, 1112.7 cm^{-1} ; MS m/z (%) 1056.5712 (M^+, 11), 596 (52.21), 504 (33.45), 470 (100), 442 (36.33), 392 (53.61), 358 (47.67), 330 (60.95), 298 (46.13), 252 (58.86), 213 (56.18), 181 (75.92), 119 (78.14), 69 (49.21).

8. Asymmetric pinacol product of (2*S*, 3a*S*, 7a*S*)-*N*-pyruvoyl-2-(*t*butyldiphenylsilyloxymethyl)indoline



1a' **2a'**

$[\alpha]_D^{25}$ = –36.51 (c = 0.49, $CHCl_3$) ; (*R,R*)-diastereomer (**2a'**) ^{1}H NMR ($CDCl_3$) δ 0.97 (s, 9H), 1.35 (s, 3H), 1.08 ~ 2.10 (m, 11H), 4.05 (m, 2H), 3.78 ~ 4.32 (m, 1H), 4.45 (m, 1H), 6.89 (s, 1H), 7.23 ~ 7.71 (m, 10H) ; ^{13}C NMR ($CDCl_3$) δ 19.24, 19.52, 19.94, 24.06, 25.88, 26.81, 29.74, 30.99, 37.20, 60.02, 66.50, 78.87, 80.21, 127.55, 129.6, 134.19, 135.73, 177.87 ; IR (NaCl) 3400 (br), 1631.9, 1605.4, 1471.8, 1391.3, 1112.5 cm^{-1} ; MS m/z (%) 928.5279 (M^+, 16), 868 (45.90), 507 (58.32), 463 (87.40), 407 (100), 362 (62.53), 332 (75.71), 290 (15.75), 267 (33.55), 198 (53.59), 134 (80.48), 68 (87.29).

9. Hydrolysis of (*S,S*)-diastereomer (**2a**) to (*S,S*)-2,3-dimethyltartaric acid (**6a**)

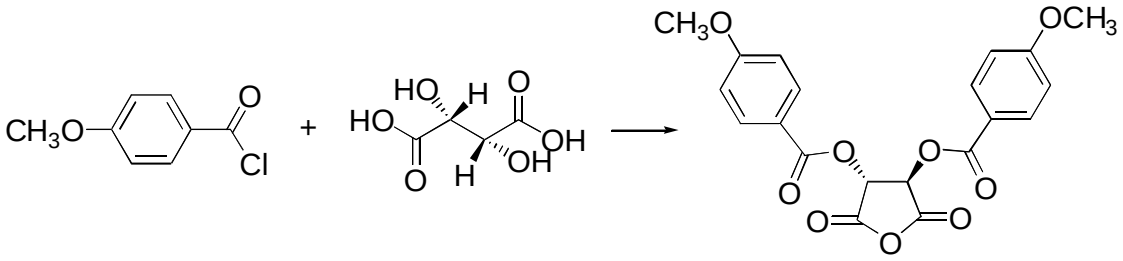
A mixture of diastereomers (135 mg, 0.288 mmol) **2a** and **3a** (S,S : S,R = 95 : 5, run 3 in Table) was dissolved in 3M HCl (5 ml) and 1,4-dioxane (5 ml). After stirred for 4h, the reaction mixture was neutralized with sat. aq. $NaHCO_3$, extracted with CH_2Cl_2 to obtain crude (*S*)-2-methoxymethylindoline (86.4 mg, 92%). The water layer was acidified with 2M aq. HCl. The solution was saturated with NaCl, extracted with EtOAc, dried over $MgSO_4$ and filtered. The filtrate was condensed under reduced pressure to

give (*S,S*)-2,3-dimethyltartaric acid (29.9 mg, 58%) ; $[\alpha]_D^{16}$ = +12.4 (c = 0.598, H_2O), [literature, $[\alpha]_D^{20}$ = +13.4 (c = 4.0, H_2O)] ; ^{1}H NMR (DMSO-d6) δ 1.36 (s, 6H), 3.0 ~ 5.5 (br, 4H) ; ^{13}C NMR (DMSO-d6) δ 21.1, 78.4, 175.3 ; IR (KBr) cm^{-1} 1161, 1266, 1726.

10. Hydrolysis of (*S,S*)-diastereomer (**2b**) to (*S,S*)-2,3-diethyltartaric acid (**6b**)

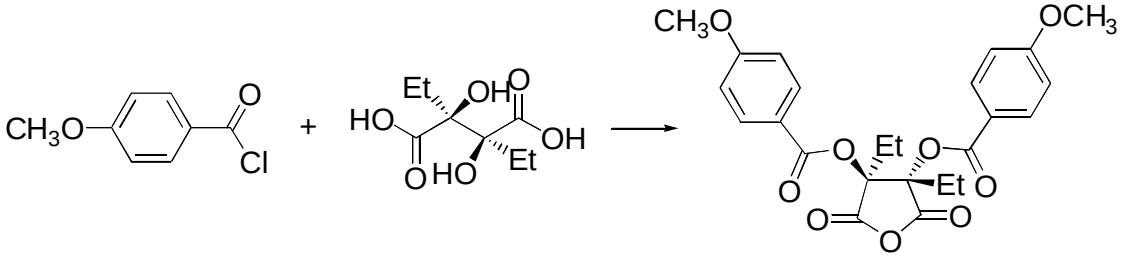
The hydrolysis was carried out under the same method as the procedure mentioned above to give (*S,S*)-2,3-diethyltartaric acid in 86 % ; $[\alpha]_D^{16}$ = –6.37 (c = 0.926, H_2O) ; ^{1}H NMR (DMSO-d6) δ 0.71 (*t*, 6H), 1.76 (m, 2H), 1.92 (m, 2H), 3.5 ~ 4.5 (br, 4H) ; ^{13}C NMR (DMSO-d6) δ 8.29, 25.5, 82.7, 174.3 ; IR (KBr) cm^{-1} 1155, 1238, 1738.

11. Synthesis of *O,O*-dianisoyltartaric acid



A mixture of L-(+)-(*R,R*)-tartaric acid (1g) and anisoyl chloride (3.41 g) was stirred for 3 h at the temperature of 150–160 ^oC. After 3 h, the solution was cooled and added to anhydrous ether (10 ml). The solution was filtered. The filtered solid was recrystallized with from ethyl acetate to give the desired product (0.33 g). ; mp : 134-135 ^oC ; $[\ ]_D^{23}$ = +172 (c = 0.65, acetone), ^{1}H NMR ($CDCl_3$) δ 3.90 (s, 6H), 6.57 (s, 2H), 7.06 ~ 7.09 (m, 4H), 8.01 ~ 8.05 (m, 4H).IR (KBr) cm^{-1} 1707, 1728, 1809.

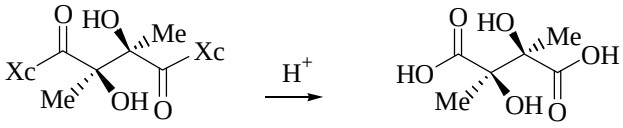
12. Synthesis of *O,O*-dianisoyl-2,3-diethyltartaric acid



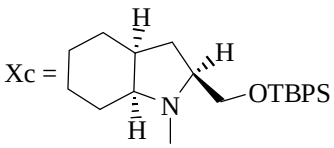
O,O-Dianisoyl-2,3-diethyltartaric acid was prepared from 2,3-diethyltartaric acid by the same method used in the preparation of *O,O*-Dianisoyltartaric acid. ^{1}H NMR (CD_2Cl_2) δ 1.25 (*t*, 6H), 2.14 (m, 4H), 3.89 (s, 6H), 6.98 ~ 7.01 (m, 4H), 8.02 (m, 4H).

13. Spectrum of *O,O*-dianisoyl-2,3-diethyltartaric acid.

14. Hydrolysis of (*R,R*)-diastereomer (**2a'**) to (*R,R*)-dimethyltartaric acid (**6a'**)



2a' (*R*,*R*) **6a'** : (*R*,*R*)-2,3-dimethyltartaric acid



The hydrolysis was carried out under the same method as the procedure mentioned above to give (*S,S*)-2,3-dimethyltartaric acid in 78 % ; $[\alpha]_D^{20}$ = –13.2 (c = 4.0, H_2O).