Supporting Information

for *N*-Spiro Chiral Quaternary Ammonium Bromides–Catalyzed Diastereo- and Enantioselective Conjugate Addition of Nitroalkanes to Cyclic α,β -Unsaturated Ketones under Phase–Transfer Conditions

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General Information. Infrared (IR) spectra were recorded on a Shimadzu IRPrestige-21 spectrometer. ^1H NMR spectra were measured on a JEOL JNM-FX400 (400 MHz) spectrometer. Chemical shifts were reported in ppm from tetramethylsilane as an internal standard. Data were reported as follows: chemical shift, integration, multiplicity (s = singlet, d = doublet, t = triplet, m = multiplet), coupling constants (Hz), and assignment. ^{13}C NMR spectra were recorded on a JEOL JNM-FX400 (100 MHz) spectrometer with complete proton decoupling. Chemical shifts are reported in ppm from the residual solvent as an internal standard. Analytical gas-liquid phase chromatography (GLC) was performed on Shimadzu GC-14B instruments equipped with a flame ionization detector using an Astec Chiradex Γ -TA (30 m $\times$ 0.25 mm) column. High performance liquid chromatography (HPLC) was performed on Shimadzu 10A instruments using 4.6 mm $\times$ 25 cm Daicel Chiralpak AD-H and AS-H. The high-resolution mass spectra (HRMS) were performed on Applied Biosystems Mariner 8295 API-TOF workstation. Optical rotation was measured on a JASCO DIP-370 digital polarimeter.

For thin layer chromatography (TLC) analysis throughout this work, Merck precoated TLC plates (silica gel 60 GF₂₅₄, 0.25 mm) were used. The products were purified by flash column chromatography on silica gel 60 (Merck 1.09386.9025, 230-400 mesh).

Cyclic α,β -unsaturated ketones **2b-d**¹ and nitroalkanes **3**^{2,3} were prepared according to the literature procedures and purified by redistillation. Other simple chemicals were purchased and used as such.

Characterization of *N*-Spiro Chiral Quaternary Ammonium Bromide (*S,S*)-1b. $[\alpha]_{\text{D}}^{26}$ 19.6° (*c* 1.02, CH₃OH); ^1H NMR (400 MHz, CDCl₃) δ 8.42 (2H, s, Ar-H), 8.14 (2H, d, *J* = 8.3 Hz, Ar-H), 7.95 (2H, s, Ar-H), 7.77 (4H, d, *J* = 8.3 Hz, Ar-H), 7.64 (4H, t, *J* = 7.1 Hz, Ar-H), 7.48 (4H, t, *J* = 7.5 Hz, Ar-H), 7.36 (4H, t, *J* = 8.3 Hz, Ar-H), 7.22–7.15 (10H, m, Ar-H), 7.04 (2H, d, *J* = 8.7 Hz, Ar-H),

6.57 (2H, d, $J = 8.3$ Hz, Ar-H), 4.88 (2H, d, $J = 14.0$ Hz, ArCH₂), 4.61 (2H, d, $J = 13.5$ Hz, ArCH₂), 4.55 (2H, d, $J = 14.0$ Hz, ArCH₂), 3.64 (2H, d, $J = 13.5$ Hz, ArCH₂); ¹³C NMR (100 MHz, C₂D₂Cl₄, 80 °C) δ 151.4 (d, $J_{\text{C-F}} = 255.7$ Hz), 141.2, 140.8, 139.7 (dt, $J_{\text{C-F}} = 254.0, 14.9$ Hz), 139.3, 137.6, 136.4, 135.6-135.3 (m), 133.8, 133.7, 133.2, 131.2, 130.8, 129.0, 128.5, 128.3, 127.8, 127.7, 127.2, 127.0, 126.3, 125.5, 124.5, 121.9, 111.6 (d, $J_{\text{C-F}} = 6.6$ Hz), 111.4 (d, $J_{\text{C-F}} = 5.8$ Hz), 62.5, 57.7; IR (neat) 3333, 3051, 3011, 2953, 1616, 1585, 1525, 1456, 1398, 1346, 1244, 1043, 910, 851, 793, 729, 665 cm⁻¹; HRMS (ESI-TOF) Calcd for C₈₀H₄₄F₁₂N: 1246.3277 (M⁺), Found: 1246.3272 (M⁺).

Representative Procedure for Catalytic Asymmetric Conjugate Addition of Nitroalkanes to Cyclic α,β -Unsaturated Ketones under Phase-Transfer Conditions (entry 7 in Table 1).

To a mixture of 2-cyclohexenone (**2a**, 28.8 mg, 0.30 mmol), chiral ammonium bromide (*S,S*)-**1b** (4.0 mg, 0.003 mmol) and Cs₂CO₃ (97.7 mg, 0.30 mmol) in toluene (6 mL) was added 1-nitropropane (**3a**, 133.9 μ L, 1.50 mmol) dropwise at -40 °C. The reaction mixture was stirred vigorously at the same temperature for 36 h. The resulting mixture was diluted with water and extracted with Et₂O. The combined extracts were washed with water and brine, and then dried over MgSO₄. Evaporation of solvents and purification of the residual crude products by column chromatography on silica gel (hexane/Et₂O = 2:1 as eluent) gave **4a**⁴ [50.4 mg, 0.27 mmol, 91% yield, *syn/anti* = 98:2, 92% ee (*syn* isomer), 37% ee (*anti* isomer)]. GLC analysis: Astec Chiradex Γ -TA (30 m $\times$ 0.25 mm) column (120 °C isotherm), retention time; *anti* isomer: 55.8 min (1'*S*^{*},3*S*^{*}) and 58.1 min (1'*R*^{*},3*R*^{*}), *syn* isomer: 62.3 min (1'*R*,3*S*) and 91.5 min (1'*S*,3*R*). The relative and absolute configurations of **4a** were determined by X-ray crystallographic analysis after derivatization to its acetal with (2*R*,3*R*)-2,3-butanediol (See S4-S6).

Characterization of the Conjugate Addition Products.

3-(1-Nitro-2-phenylethyl)cyclohexanone (4b). >95:5 *syn/anti* mixture. ¹H NMR (400 MHz, CDCl₃) δ 7.34-7.23 (3H, m, Ar-H), 7.18-7.12 (2H, m, Ar-H), 4.69 (1H, ddd, $J = 5.1, 9.9, 9.9$ Hz, CHNO₂ (*syn*)), 4.61 (1H, ddd, $J = 4.4, 7.1, 10.7$ Hz, CHNO₂ (*anti*)), 3.27 (1H, dd, $J = 10.4, 14.4$ Hz, CHCHNO₂), 3.09 (1H, dd, $J = 4.4, 14.4$ Hz, CHCHNO₂), 2.53-2.48 (1H, m, COCH₂), 2.47-2.40 (1H, m, COCH₂), 2.34-2.23 (3H, m, COCH₂ and CHCHNO₂), 2.19-2.11 (1H, m, CH₂), 2.10-2.03 (1H, m, CH₂), 1.73-1.61 (1H, m, CH₂), 1.59-1.49 (1H, m, CH₂); ¹³C NMR (100 MHz, CDCl₃) δ 208.0, 135.0, 128.8, 128.5, 127.3, 93.6, 43.1, 41.3, 40.9, 36.8, 28.1, 24.5 (*syn* isomer); 208.1, 135.0, 129.2, 128.8, 128.8, 93.7, 44.3, 41.6, 41.0, 37.0, 27.2, 24.3 (*anti* isomer); IR (neat) 3030, 2940, 2824, 1713, 1545, 1447, 1373, 1318, 1234, 1032, 858, 756, 702 cm⁻¹; HRMS (ESI-TOF) Calcd for C₁₄H₁₈NO₃: 248.1281 ([M+H]⁺), Found: 248.1292 ([M+H]⁺); HPLC analysis: DAICEL Chiralpak AD-H, hexane/ethanol = 10:1, flow rate = 1.0 mL/min, $\lambda = 220$ nm, retention time; *anti* isomer: 65.7 min (major) and 94.8 min (minor), *syn* isomer: 70.3 min (major) and 103.8 min (minor).

3-(2-Methyl-1-nitropropyl)cyclohexanone (4c). >95:5 *syn/anti* mixture. ^1H NMR (400 MHz, CDCl_3) δ 4.24 (1H, dd, $J = 5.5, 9.1$ Hz, CHNO_2 (*syn*)), 4.21 (1H, dd, $J = 7.1, 7.1$ Hz, CHNO_2 (*anti*)), 2.50-2.39 (2H, m, CH_2), 2.41 (1H, dd, $J = 13.9, 13.9$ Hz, COCH_2), 2.36-2.21 (3H, m, $\text{CH}(\text{CH}_3)_2$, COCH_2 and CHCHNO_2), 2.17-2.10 (1H, m, CH_2), 1.99-1.92 (1H, m, CH_2), 1.68 (1H, ddt, $J = 3.9, 13.5, 25.7$ Hz, CH_2), 1.39 (1H, ddd, $J = 3.6, 12.8, 24.8$ Hz, CH_2), 1.00 (3H, d, $J = 4.8$ Hz, CH_3), 0.99 (3H, d, $J = 4.4$ Hz, CH_3); ^{13}C NMR (100 MHz, CDCl_3) δ 208.9, 97.9, 41.9, 41.0, 38.5, 28.5, 28.4, 24.7, 18.7, 18.6 (*syn* isomer); 208.8, 97.7, 44.3, 41.1, 38.8, 28.4, 26.5, 24.5, 19.2, 17.4 (*anti* isomer); IR (neat) 2966, 2924, 2854, 1715, 1541, 1456, 1363, 1231, 758, 706 cm^{-1} ; HRMS (ESI-TOF) Calcd for $\text{C}_{10}\text{H}_{18}\text{NO}_3$: 200.1281 ($[\text{M}+\text{H}]^+$), Found: 200.1285 ($[\text{M}+\text{H}]^+$); HPLC analysis: DAICEL Chiralpak AS-H, hexane/2-propanol = 9:1, flow rate = 0.5 mL/min, $\lambda = 220$ nm, retention time; *syn* isomer: 21.8 min (minor) and 32.0 min (major), *anti* isomer: 26.0 min (minor) and 42.4 min (major).

3-(2-Cyclohexyl-1-nitroethyl)cyclohexanone (4e). 95:5 *syn/anti* mixture. ^1H NMR (400 MHz, CDCl_3) δ 4.56 (1H, ddd, $J = 3.6, 5.9, 11.1$ Hz, CHNO_2 (*syn*)), 4.50 (1H, ddd, $J = 3.2, 7.9, 11.1$ Hz, CHNO_2 (*anti*)), 2.46-2.38 (2H, m, COCH_2), 2.30-2.19 (3H, m, CHCHNO_2 and COCH_2), 2.17-2.09 (1H, m, CH_2), 2.04-1.96 (2H, m, CH_2), 1.86-1.81 (1H, m, CH_2), 1.74-1.59 (5H, m, CH_2), 1.55-1.37 (2H, m, CH_2), 1.28-1.08 (4H, m, CH_2), 1.00-0.80 (2H, m, CH_2); ^{13}C NMR (100 MHz, CDCl_3) δ 208.3, 90.1, 43.3, 41.9, 40.9, 38.2, 34.5, 33.7, 32.1, 27.9, 26.3, 26.0, 25.8, 24.4 (*syn* isomer); 214.7, 90.2, 44.1, 42.2, 41.0, 38.3, 34.5, 33.8, 32.1, 28.0, 26.0, 25.8, 24.5 (*anti* isomer); IR (neat) 2920, 2851, 1713, 1543, 1446, 1337, 1310, 1229, 1063, 947, 835, 660 cm^{-1} ; HRMS (ESI-TOF) Calcd for $\text{C}_{14}\text{H}_{23}\text{NO}_3\text{Na}$: 276.1570 ($[\text{M}+\text{Na}]^+$), Found: 276.1577 ($[\text{M}+\text{Na}]^+$); HPLC analysis: DAICEL Chiralpak AD-H, hexane/2-propanol = 10:1, flow rate = 0.5 mL/min, $\lambda = 220$ nm, retention time; *anti* isomer: 22.6 min (major) and 27.0 min (minor), *syn* isomer: 24.8 min (minor) and 30.3 min (major).

3-(1-Nitropropyl)cycloheptanone (4g). 88:12 *syn/anti* mixture. ^1H NMR (400 MHz, CDCl_3) δ 4.49 (1H, ddd, $J = 4.0, 5.9, 10.3$ Hz, CHNO_2 (*syn*)), 4.47 (1H, ddd, $J = 6.7, 6.7, 13.9$ Hz, CHNO_2 (*anti*)), 2.57-2.43 (4H, m, COCH_2), 2.23-2.14 (1H, m, CHCHNO_2), 2.12-1.90 (4H, m, CH_2), 1.85-1.74 (1H, m, CH_2), 1.66-1.56 (1H, m, CH_2), 1.48-1.30 (2H, m, CH_2), 0.98 (3H, t, $J = 7.1$ Hz, CH_3); ^{13}C NMR (100 MHz, CDCl_3) δ 211.3, 94.4, 45.1, 43.5, 39.3, 32.9, 28.1, 24.1, 24.0, 10.6 (*syn* isomer); 206.6, 94.2, 45.6, 43.6, 39.1, 32.6, 27.8, 24.2, 24.1, 10.5 (*anti* isomer); IR (neat) 2924, 2854, 1703, 1544, 1460, 1371, 1259, 1143, 1029, 937, 806 cm^{-1} ; HRMS (ESI-TOF) Calcd for $\text{C}_{10}\text{H}_{18}\text{NO}_3$: 200.1281 ($[\text{M}+\text{H}]^+$), Found: 200.1286 ($[\text{M}+\text{H}]^+$); HPLC analysis: DAICEL Chiralpak AD-H, hexane/2-propanol = 10:1, flow rate = 0.5 mL/min, $\lambda = 220$ nm, retention time; *anti* isomer: 28.6 min (minor) and 30.7 min (major), *syn* isomer: 37.8 min (minor) and 42.8 min (major).

3-(1-Nitropropyl)cyclooctanone (4h). 64:36 *syn/anti* mixture. ^1H NMR (400 MHz, CDCl_3), δ 4.36 (1H, ddd, $J = 4.0, 5.9, 10.3$ Hz, CHNO_2), 2.53 (1H, dd, $J = 11.9, 24.1$ Hz, COCH_2), 2.50-2.34 (3H, m, CH_2), 2.31-2.26 (1H, m, CHCHNO_2), 2.09-1.97 (1H, m, CH_2), 1.95-1.65 (5H, m, CH_2), 1.56-1.43 (2H, m, CH_2), 1.41-1.26 (2H, m, CH_2), 0.98 (3H, t, $J = 7.5$ Hz, CH_3 (*syn*)), 0.98 (3H, t, $J = 7.5$ Hz, CH_3 (*anti*)); ^{13}C NMR (100 MHz, CDCl_3) δ 214.4, 94.6, 42.9, 42.2, 40.7, 29.8, 27.3, 24.5, 24.5, 23.3, 10.4 (*syn* isomer); 214.1, 94.3, 43.1, 42.6, 40.9, 28.8, 27.4, 24.2, 24.1, 22.9, 10.5 (*anti* isomer); IR (neat) 2935, 2860, 1699, 1543, 1463, 1373, 1325, 1242, 1103, 925, 810, 752, 667 cm^{-1} ; HRMS (ESI-TOF) Calcd for $\text{C}_{11}\text{H}_{20}\text{NO}_3$: 214.1438 ($[\text{M}+\text{H}]^+$), Found: 214.1441 ($[\text{M}+\text{H}]^+$); HPLC analysis: DAICEL Chiralpak AS-H, hexane/2-propanol = 50:1, flow rate = 1.0 mL/min, $\lambda = 220$ nm, retention time; *syn* isomer: 38.9 min (minor) and 44.6 min (major), *anti* isomer: 62.6 min (major) and 72.5 min (minor).

6-(1-Nitropropyl)-1,4-dioxaspiro[4.5]decan-8-one (4i). >95:5 *syn/anti* mixture. ^1H NMR (400 MHz, CDCl_3), δ 4.85 (1H, ddd, $J = 3.2, 3.2, 10.7$ Hz, CHNO_2), 4.21-3.95 (4H, m, CH_2O), 2.92 (1H, dd, $J = 13.8$ Hz, COCH_2), 2.67-2.58 (2H, m, CH_2), 2.41-2.33 (2H, m, CH_2), 2.11-2.00 (2H, m, CH_2), 1.77 (1H, dt, $J = 5.1, 13.8$ Hz, CHCHNO_2), 1.72-1.62 (2H, m, CH_2), 0.95 (3H, t, $J = 7.1$ Hz, CH_3), ^{13}C NMR (100 MHz, CDCl_3) δ 207.9, 107.4, 86.6, 65.2, 64.6, 46.4, 39.2, 38.0, 32.9, 25.7, 10.5 (*syn* isomer); 207.7, 108.1, 86.3, 64.9, 64.0, 42.4, 40.0, 37.6, 33.5, 25.7, 10.5 (*anti* isomer); IR (neat) 2970, 2897, 1219, 1549, 1377, 1346, 1279, 1217, 1121, 1086, 1020, 951, 916, 808 cm^{-1} ; HRMS (ESI-TOF) Calcd for $\text{C}_{11}\text{H}_{18}\text{NO}_5$: 244.1179 ($[\text{M}+\text{H}]^+$), Found: 244.1182 ($[\text{M}+\text{H}]^+$); HPLC analysis: DAICEL Chiralpak AD-H, hexane/2-propanol = 10:1, flow rate = 0.5 mL/min, $\lambda = 220$ nm, retention time; *syn* isomer: 22.2 min (minor) and 28.4 min (major), *anti* isomer: 33.6 min (minor) and 40.3 min (major).

Assignment of the Absolute and Relative Configurations of γ -Nitro Ketone 4a.

To a solution of γ -nitro ketone **4a** (185.2 mg, 1.0 mmol) in benzene (10 mL) was added (2*R*,3*R*)-2,3-butanediol (365.2 μL , 4.0 mmol) and catalytic amount of *p*-toluenesulfonic acid. Then, the mixture was heated at 100 $^\circ\text{C}$ for 4 h. After being cooled to room temperature, the resulting mixture was diluted with water and extracted with Et_2O . The combined extracts were washed with water and brine, and then dried over MgSO_4 . Evaporation of solvents and purification of the residual crude products

by column chromatography on silica gel (hexane/AcOEt = 10:1 as eluent) afforded **5** (236.9 mg, 0.92 mmol, 92% yield) as a colorless solid. Recrystallization of **5** was conducted from Et₂O. $[\alpha]_D^{26}$ 13.3° (*c* 1.02, CHCl₃); ¹H NMR (400 MHz, CDCl₃), δ 4.24 (1H, ddd, *J* = 3.6, 7.9, 11.1 Hz, CHNO₂), 3.64-3.55 (2H, m, OCH), 2.12-2.14 (1H, m, CH₂), 2.00-1.92 (1H, m, CH₂), 1.86-1.67 (5H, m, CH₂), 1.63-1.53 (1H, m, CH₂), 1.44 (1H, dt, *J* = 3.6, 12.3 Hz, CHNO₂), 1.35 (1H, t, *J* = 12.3 Hz, CH₂), 1.22 (3H, d, *J* = 5.5 Hz, CH₃), 1.21 (3H, d, *J* = 5.5 Hz, CH₃), 1.03-0.97 (1H, m, CH₂), 0.94 (3H, t, *J* = 7.5 Hz, CH₃); ¹³C NMR (100 MHz, CDCl₃) δ 107.2, 95.0, 78.3, 77.8, 39.6, 38.6, 35.8, 27.8, 24.2, 22.6, 17.0, 16.9, 10.5; IR (neat) 2972, 2937, 2868, 1546, 1454, 1375, 1313, 1292, 1093, 977, 806 cm⁻¹; HRMS (ESI-TOF) Calcd for C₁₃H₂₃NO₄Na: 280.1519 ([M+Na]⁺), Found: 280.1522 ([M+Na]⁺).

X-ray Structure Determination

The single crystal of **5** was mounted on a CryoLoop (Hampton Research Co. Ltd.). Data of X-ray diffraction were collected by a Rigaku RAXIS-RAPID Imaging Plate two-dimensional area detector using graphite-monochromated MoK α radiation (λ = 0.71075 Å) to a maximum 2 θ value of 54.9°. All of the crystallographic calculations were performed using CrystalStructure software package of the Rigaku Corporation and Molecular Structure Corporation. The crystal structure was solved by the direct methods using SIR2002, and refined by the full-matrix least squares using SHELXL97. All non-hydrogen atoms and hydrogen atoms were refined anisotropically and isotropically, respectively. The crystallographic data are summarized in the following table.

Experimental Details			
empirical formula	C ₁₃ H ₂₃ NO ₄	<i>T</i> , °C	23.0
formula weight	257.33	μ (MoK α), cm ⁻¹	0.860
crystal system	orthorhombic	no. of reflns meased	2075
space group	P2 ₁ 2 ₁ 2 ₁ (#19)	no. of reflns obsd	3304
<i>a</i> , Å	9.258 (3)	no. of variable	164
<i>b</i> , Å	10.015 (4)	<i>R</i> <i>I</i>	0.0371
<i>c</i> , Å	15.701 (7)	<i>R</i> _w	0.0763
<i>V</i> , Å ³	1455.8 (10)	Goodness of fit	0.577
<i>Z</i>	4	Max shift/error in final cycle	0.000
<i>D</i> _{calc} , g/cm ³	1.174

ORTEP Diagram of 5

References

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Copies of ^1H and ^{13}C NMR Spectra of Chiral Quaternary Ammonium Salt 1b and Conjugate Addition Products 4b-4i.

ST5701.F3ohphNAS.C2D2Cl4