Supporting Text

General Procedures

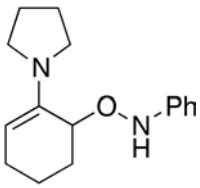
Anhydrous solvents were purchased from ACROS or Kanto for the reaction. Acetonitrile was dried with molecular sieves 4A, 4-8 mesh, before use. Nitrosobenzene was purchased from Tokyo Chemical Industry. 1-Pyrrolidino-1-cyclohexene and aldehydes for the reaction were distilled before use. Ketones for the reaction were purchased from Aldrich. Purification of reaction products was carried out by flash column chromatography using silica gel 60 (Merck 230-400 mesh) and Florisil (Wako Pure Chemical or Fisher 60-100 mesh). Analytical thin layer chromatography (TLC) was performed on Merck precoated (0.25 mm) silica gel 60-F_{254} plates. Visualization was accomplished with UV light and phosphomolybdic acid solution in ethanol by heating.

Infrared (IR) spectra were recorded on a Shimadzu FTIR-8100 spectrometer or Nicolet 20 SXB FTIR. ^{1}H NMR spectra were recorded on a Varian Gemini-300 (300 MHz) spectrometer or Bruker DRX-500 (500 MHz) or 400 (400 MHz) at ambient temperature. Data are reported as follows: chemical shift in ppm from internal standard tetramethylsilane on the δ scale, multiplicity (b = broad, s = singlet, d = doublet, t = triplet, q = quartet, and m = multiplet), integration, coupling constant (Hz), and assignment. ^{13}C NMR was recorded on a Varian Gemini-300 (75 MHz) spectrometer or Bruker DRX-500 (125 MHz) or 400 (100 MHz) at ambient temperature. Chemical shifts are reported in ppm from tetramethylsilane on the δ scale, with solvent resonance used as internal standard (deuterochloroform at 77.0 ppm). High-performance liquid chromatography (HPLC) was performed on a Shimadzu 10A or Varian ProStar Series equipped with a variable wavelength detector using a Chiralcel AD, AD-H, or OD-H column (0.46 × 25 cm) from Daicel. Optical rotations were measured on a JASCO DIP-1000 polarimeter and reported as follows: $[\alpha]_{\lambda}^{T^{\circ}C}$($c$ = g/100 ml, solvent). Mass spectra were obtained on QSTAR (Applied SCIEX Biochemistry/MDS) spectrometers and JMS700 (JEOL) spectrometers at the Chemical Instrument Center and Graduate School of Engineering at Nagoya University (Nagoya, Japan) or a Kratos MS-30 at the University of Chicago Department of Chemistry (Chicago). Elemental analysis was measured at the Graduate school of Agriculture at Nagoya University.

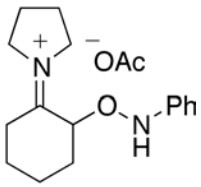
General procedure for the reaction of 1-pyrrolidino-1-cyclohexene with nitrosobenzene. To a test tube equipped with a magnetic stir bar and charged with nitrosobenzene (1 eq, 53.6 mg, 0.5 mmol) was added anhydrous benzene (1 ml), and the resulting mixture was stirred at room temperature for 20 min. After cooling to 0°C, 1-pyrrolidino-1-cyclohexene (1 eq, 80 μl, 0.5 mmol) was added and stirred at this temperature for 15 min. Then, acetic acid (1 eq, 28 μl, 0.5 mmol) was added at 0°C and stirred at this temperature for 15 min. The reaction mixture was quenched by iced, saturated NH_4Cl solution (10 ml), and the aqueous layer was extracted with ethyl acetate (20 ml, three times). The combined organic extracts were washed with brine, dried over Na_2SO_4 with cooling, and concentrated under reduced pressure after filtration. The residual crude product was chromatographed with cooling on a two-layered column filled

with Florisil (upper layer) and silica gel (lower layer) using a mixture of ethyl acetate and hexane as the eluant to give the *O*-adduct.

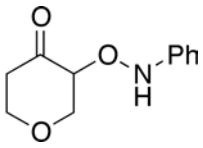
NMR Study for the Reaction of 1-Pyrrolidino-1-cyclohexene with Nitrosobenzene. To an NMR tube charged with DMSO-d_6 containing 1% (vol/vol) tetramethylsilane solution (500 μl) of nitrosobenzene (1 eq, 26.8 mg, 0.25 mmol) was added 1-pyrrolidino-1-cyclohexene (1 eq, 40 μl, 0.25 mmol) at room temperature. After 10 min, NMR was taken at room temperature. Then, acetic acid (1eq, 14 μl, 0.25 mmol) was added to this mixture, and NMR was taken again.



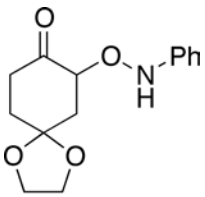
2-(*N*-phenyl Aminooxy)-1-pyrrolidino-1-cyclohexene (Intermediate 1; Fig. 1). ^{1}H NMR [DMSO-d_6, contains 1% (vol/vol) tetramethylsilane solution, 400 MHz] δ8.17 (s, 1H, N*H*), 7.17 (t, 2H, *J* = 7.0 Hz, Ar-*H*), 7.04 (d, 2H, *J* = 7.6 Hz, Ar-*H*), 6.75 (t, 1H, *J* = 6.9 Hz, Ar-*H*), 4.43 (t, 1H, *J* = 3.9 Hz, C*H*), 4.32 (t, 1H, *J* =4.5 Hz, C*H*), 3.15–3.20 (m, 2H, CH_2), 2.90–2.95 (m, 4H, CH_2), 1.84–2.08 (m, 6H, CH_2), 1.70–1.74 (m, 4H, CH_2).



2-(*N*-phenyl aminooxy)-1-cyclohexylidene-1-pyrrolidinium (Intermediate 2; Fig. 1). ^{1}H NMR [DMSO-d_6, contains 1% (vol/vol) tetramethylsilane solution, 400 MHz] δ7.28 (t, 2H, *J* = 7.9 Hz, Ar-*H*), 6.99 (t, 1H, *J* = 7.4 Hz, Ar-*H*), 6.64 (d, 1H, *J* = 7.3 Hz, Ar-*H*), 5.31 (t, 1H, *J* = 4.4 Hz, C*H*), 3.15–3.20 (m, 2H, CH_2), 2.98–3.07 (m, 6H, CH_2), 2.20–2.26 (m, 6H, CH_2), 1.72–1.73 (m, 2H, CH_2), 1.60–1.64 (m, 2H, CH_2).

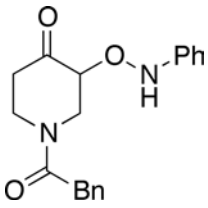


2-(*N*-phenyl aminooxy)tetrahydro-4*H*-pyran-4-one (5b; Table 2, Entry 2). Purification by flash column chromatography with elution by hexane/ethyl acetate (5:1) provided a yellowish powder. TLC R_f = 0.079 (5:1 hexane/ethyl acetate); $[\alpha]_D^{27}$ + 63.0° (*c* = 0.2, $CHCl_3$); IR ($CHCl_3$) 3,262, 2,990, 2,886, 1,708, 1,659, 1,587, 1,478, 1,273, 1,125, 1,081, 988, 968, 860 cm^{-1}; ^{1}H NMR ($CDCl_3$, 400 MHz) δ7.77 (s, 1H, N*H*), 7.26 (t, 2H, *J* = 7.8 Hz, Ar-*H*), 6.97 (t, 1H, *J* = 7.4 Hz, Ar-*H*), 6.92 (d, 2H, *J* = 7.8 Hz, Ar-*H*), 4.48–4.52 (m, 1H, CH_2), 4.40–4.45 (m, 1H, CH_2) 4.16–4.19 (m, 1H, C*H*), 3.66–3.74 (m, 2H, CH_2), 2.66–2.71 (m, 1H, CH_2), 2.57 (td, 1H, *J* = 2.9, 14.3 CH_2); ^{13}C NMR ($CDCl_3$, 100 MHz) δ205.4, 147.7, 128.9 (2C), 122.5, 114.7 (2C), 83.5, 70.0, 68.1, 42.3; MS (chemical ionization) exact mass calcd for $C_{11}H_{13}NO_3$ $(M + H)^+$: 208.1. Found: 208.1. Enantiomeric excess was determined by HPLC with a Chiralcel AD-H column (9:1 hexane/2-propanol), 1.0 ml/min; major enantiomer t_r = 19.8 min; minor enantiomer t_r = 26.5 min.

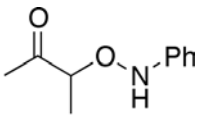


7-(*N*-phenyl aminooxy)-1,4-dioxa-spiro[4.5]decan-8-one (5c; Table 2, Entry 3). Purification by flash column chromatography with elution by hexane/ethyl acetate (7:1) provided a yellowish powder. TLC R_f = 0.18 (3:1 hexane/ethyl acetate); $[\alpha]_D^{27}$ + 40.6° (*c* = 2.3, $CHCl_3$); IR ($CHCl_3$) 3,164, 2,989, 1,855, 1,764, 1,580, 1,382, 861 cm^{-1}; ^{1}H NMR

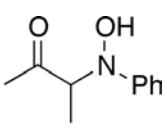
($CDCl_3$, 400 MHz) δ7.84 (s, 1H, N*H*), 7.24 (t, 2H, *J* = 7.5 Hz, Ar-*H*), 6.92 (t, 3H, *J* = 8.1 Hz, Ar-*H*), 4.64 (q, 1H, *J* = 5.7 Hz, C*H*), 4.05 (s, 4H, CH_2), 2.65–2.81 (m, 1H, CH_2), 2.42–2.50 (m, 4H, CH_2), 1.99–2.05 (m, 1H, CH_2); ^{13}C NMR ($CDCl_3$, 100 MHz) δ210.3, 147.9, 128.8 (2C), 122.0, 114.3 (2C), 107.5, 82.6, 64.6, 64.5, 39.6, 35.9, 34.3; MS (chemical ionization) exact mass calcd for $C_{14}H_{17}NO_4$ $(M + H)^+$: 264.0. Found: 264.10. Enantiomeric excess was determined by HPLC with a Chiralcel OD-H column (9:1 hexane/2-propanol), 0.5 ml/min; major enantiomer t_r = 20.2 min; minor enantiomer t_r = 23.2 min.



1-Phenylacethyl-3-(*N*-phenyl aminooxy)piperidin-4-one (5d; Table 2, Entry 4). Purification by flash column chromatography with elution by hexane/ethyl acetate (3:1) provided a yellowish oil. TLC R_f = 0.10 (2:1 hexane/ethyl acetate); $[\alpha]_D^{30}$ + 25.7° (*c* = 0.7, $CHCl_3$); IR (neat) 3,269, 3,033, 2,954, 1,710, 1,649, 1,547, 1,480, 1,411, 1,365, 1,277, 1,110, 986, 910 cm^{-1}; ^{1}H NMR ($CDCl_3$, 400 MHz) δ7.75 (bs, 1H, N*H*), 7.25–7.37 (m, 8H, Ar-*H*), 7.22 (t, 2H, *J* = 7.5 Hz, Ar-*H*), 6.94 (t, 2H, *J* = 7.4 Hz, Ar-*H*), 4.36 (b, 1H, C*H*), 3.75 (t, 2H, CH_2), 3.55 (q, 1H, CH_2), 3.37–3.44 (m, 1H, CH_2), 2.55 (b, 2H, CH_2), 2.41(b, 2H, CH_2); ^{13}C NMR ($CDCl_3$, 100 MHz) δ205.4, 155.1, 136.4, 128.8 (3C), 128.4, 128.2, 127.9 (2C), 122.3, 114.5 (2C), 82.9, 67.9, 64.5, 47.0, 43.7, 42.9, 40.8; MS (chemical ionization) exact mass calcd for $C_{19}H_{20}N_2O_3$ $(M - H)^+$: 323.1. Found: 323.1. Enantiomeric excess was determined by HPLC with a Chiralcel AD-H column (9:1 hexane/2-propanol), 1.0 ml/min; major enantiomer t_r = 36.5 min; minor enantiomer t_r = 26.0 min.

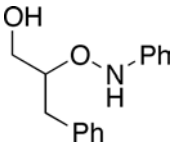


3-(*N*-phenyl aminooxy)butan-2-one (5e; Table 2, Entry 5). Purification by flash column chromatography with elution by hexane/ethyl acetate (10:1) provided a yellowish oil. TLC R_f = 0.20 (5:1 hexane/ethyl acetate); $[\alpha]_D^{25}$ + 57.4° (*c* = 3.8, $CHCl_3$); IR (neat) 3,572, 1,815, 1,765, 1,711, 1,582, 1,484, 1,382, 837, 780 cm^{-1}; ^{1}H NMR ($CDCl_3$, 400 MHz) δ7.37 (s, 1H, N*H*), 7.26 (t, 2H, *J* = 7.4 Hz, Ar-*H*), 6.96 (t, 3H, *J* = 8.5 Hz, Ar-*H*), 4.43 (q, 1H, C*H*), 2.20 (s, 3H, CH_3), 1.42 (d, 3H, *J* = 7.0 Hz, CH_3); ^{13}C NMR ($CDCl_3$, 100 MHz) δ209.6, 148.2, 129.3 (2C), 122.7, 114.8 (2C), 84.8, 25.9, 15.8; MS (electron impact ionization) exact mass calcd for $C_{10}H_{13}NO_2$ (M): 179. Found: 179. Enantiomeric excess was determined by HPLC with a Chiralcel AD-H column (40:1 hexane/2-propanol), 0.5 ml/min; major enantiomer t_r = 45.2 min; minor enantiomer t_r = 47.6 min.

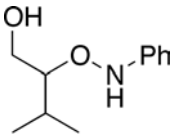


3-(*N*-phenyl hydroxyamino)butan-2-one (7e; Table 2, Entry 5). Purification by flash column chromatography with elution by hexane/ethyl acetate (10:1) provided a yellowish oil. TLC R_f = 0.15 (5:1 hexane/ethyl acetate); $[\alpha]_D^{25}$ – 6.3° (*c* = 0.12, $CHCl_3$); IR (neat) 3,623, 3,141, 1,855, 1,659, 1,580, 1,468, 1,291, 1,161, 852 cm^{-1}; ^{1}H NMR ($CDCl_3$, 400 MHz) δ7.32 (t, 2H, *J* = 7.4 Hz, Ar-*H*), 7.10 (d, 2H, *J* = 7.7 Hz, Ar-*H*), 6.97 (t, 1H, *J* = 7.6 Hz, Ar-*H*), 5.80 (s, 1H, N-O*H*), 4.24 (q, 1H, *J* = 7.6 Hz, C*H*), 2.26 (s, 3H, CH_3), 1.31 (d, 3H, *J* = 6.7 Hz, CH_3); ^{13}C NMR ($CDCl_3$, 100 MHz) δ209.4, 150.7, 129.3 (2C), 122.3, 116.5 (2C), 69.98, 27.4, 10.8; MS (electron impact) exact mass calcd for $C_{10}H_{13}NO_2$ (M): 179. Found: 179. Enantiomeric excess was determined by HPLC with a Chiralcel AD-H column (40:1

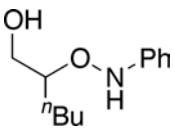
hexane/2-propanol), 0.5 ml/min; major enantiomer t_r = 28.9 min; minor enantiomer t_r = 25.9 min.



3-Phenyl-2-(*N*-phenyl aminooxy)-propan-1-ol (5f; Table 2, Entry 6). Purification by flash column chromatography with elution by hexane/ethyl acetate (6:1) provided a yellowish oil. TLC R_f = 0.27 (2:1 hexane/ethyl acetate); $[\alpha]_D^{20}$ + 26.0 (c = 1.07, $CHCl_3$); IR (neat) 3,314, 2,976, 2,862, 1,599, 1,491, 1,452, 1,402, 1,250, 1,105, 1,039, 9,10.5; ^{1}H δ7.40-7.12 (m, 8H), 6.94 (t, J = 7.2 Hz, 1H), 6.82 (dd, J = 0.9, 8.7 Hz, 1H), 4.13 (dddd, J = 2.7, 6.9, 6.3, 6.3 Hz, 1H), 3.85 (dd, J = 2.7, 12 Hz, 1H), 3.71 (dd, J = 5.7, 12 Hz, 1H), 3.04 (dd, J = 6.9, 13.8 Hz, 1H), 2.84 (dd, J = 6.9, 13.8 Hz, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ148.2, 137.7, 129.4, 128.9, 128.4, 126.4, 122.3, 114.5, 84.9, 64.1, 36.3; high-resolution MS exact mass calcd for ($C_{12}H_{17}NO_2$) requires m/z 243.1259, found m/z 243.1251. Enantiomeric excess was determined by HPLC with a Chiralcel AD column (95:5 hexane/ethanol), 1.0 ml/min; major enantiomer t_r = 42.8 min; minor enantiomer t_r = 40.1 min.



3-Methyl-2-(*N*-phenyl aminooxy)butan-1-ol (5g; Table 2, Entry 7). Purification by flash column chromatography with elution by hexane/ethyl acetate (4:1) provided a yellowish oil. TLC R_f = 0.22 (2:1 hexane/ethyl acetate); $[\alpha]_D^{20}$ + 18.3 (c = 1.03, $CHCl_3$); IR (neat) 3,400, 3,269, 3,047, 2,963, 2,878, 1,599, 1,491, 1,468, 1,412, 1,238, 1,051, 1,024, 978.0, 908.6, 771.6, 735.0, 694.5 cm^{-1}; ^{1}H NMR (300 MHz) δ7.38–7.20 (m, 3H), 7.10–6.95 (m, 3H), 3.92–3.85 (m, 2H), 3.80–3.70 (m, 1H), 2.65 (t, J = 5.7 Hz, 1H), 2.12–1.95 (m, 1H), 1.05 (d, J = 6.9 Hz, 3H), 1.01 (d, J = 6.9 Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ148.2, 128.9, 122.3, 114.8, 88.5, 63.4, 28.6, 18.7, 18.5; high-resolution MS exact mass calcd for ($C_{11}H_{17}NO_2$) requires m/z 195.1259, found m/z 195.1239. Enantiomeric excess was determined by HPLC with a Chiralcel AD column (95:5 hexane/ethanol), 1.0 ml/min; major enantiomer t_r = 16.2 min; minor enantiomer t_r =14.8 min.



2-(*N*-phenyl aminooxy)-hexan-1-ol (5h; Table 2, Entry 8). Purification by flash column chromatography with elution by hexane/ethyl acetate (6:1) provided a yellowish oil. TLC R_f = 0.36 (2:1 hexane/ethyl acetate); $[\alpha]_D^{20}$ + 14.1 (c = 1.08, $CHCl_3$); IR (neat) 3,377, 3,144, 2,955, 1,601, 1,493, 1,464, 1,377, 1,240, 1,030, 902.8, 769.7; ^{1}H NMR (300 MHz, $CDCl_3$) δ7.34–7.20 (m, 2H), 7.04–6.94 (m, 3H), 3.96 (dddd, J = 2.4, 6.6, 6.6, 6.6 Hz, 1H), 3.91–3.72 (m, 2H), 2.48 (m, 1H), 1.80–1.20 (m, 7H), 0.92 (t, J = 6.6 Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ148.3, 128.8, 122.1, 114.5, 83.8, 64.9, 29.5, 27.8, 22.7, 13.8; high-resolution MS exact mass calcd for ($C_{12}H_{19}NO_2$) requires m/z 209.1416, found m/z 209.1401. Enantiomeric excess was determined by HPLC with a Chiralcel AD column (95:5 hexane/ethanol), 1.0 ml/min; major enantiomer t_r = 19.5 min; minor enantiomer t_r =17.9 min.

Crystallographic Experimental Procudures

Data Collection. A plate-shaped fragment (0.40 × 0.25 × 0.05 mm) was selected under a stereomicroscope while immersed in Fluorolube oil to avoid possible reaction with air.

The crystal was removed from the oil by using a tapered glass fiber that also served to hold the crystal for data collection. The crystal was mounted and centered on a Bruker SMART APEX system at 100 K. Rotation and still images showed the diffractions to be sharp. Frames separated in reciprocal space were obtained and provided an orientation matrix and initial cell parameters. Final cell parameters were obtained from the full data set.

A "full-sphere" data set was obtained that samples approximately all reciprocal space to a resolution of 0.84 Å using 0.3° steps in ω using 15-sec integration times for each frame. Data collection was made at 100 K. Integration of intensities and refinement of cell parameters were performed by using SAINT.* Absorption corrections were applied by using SADABS* based on redundant diffractions.

Structure Solution and Refinement. The space group was determined as $P2_1$ based on systematic absences and intensity statistics. Direct methods were used to locate the Br atom and many C from the E map. Repeated-difference Fourier maps allowed recognition of all expected C, N, and O atoms. After anisotropic refinement of all non-H atoms, ideal H atom positions were calculated. Final refinement was anisotropic for Br, C, N, and O atoms and isotropic riding for H atoms. No anomalous bond lengths or thermal parameters were noted. All ORTEP diagrams were drawn with 50% probability ellipsoids.

Equations of Interest:

$R_{int} = \Sigma|F_o^2 - \langle F_o^2 \rangle|/\Sigma|F_o^2|$ $\qquad$ $R1 = \Sigma||F_o| - |F_c||/\Sigma|F_o|$

$wR2 = \{\Sigma\,[w(F_o^2 - F_c^2)^2]/\Sigma\,[w\,(F_o^2)^2]\}^{1/2}$ $\qquad$ $\text{GooF} = S = \{\Sigma\,[w(F_o^2 - F_c^2)^2]/(n-p)^{1/2}\}$

where: $w = q/\sigma^2\,(F_o^2) + (aP)^2 + bP$, $n =$ number of independent reflections, and $p =$ number of parameters refined; q, a, b, and P are as defined.*

*All software and sources of scattering factors are contained in the SHELXTL 5.1 program library (G. Sheldrick, Bruker Analytical X-ray Systems, Madison, WI).