

Supporting Information

To accompany

Kinetic Resolution of Racemic Amines Using the Provisional Chirality Generated by Spontaneous Crystallization

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General experimental:

General. NMR spectra were recorded on CDCl₃ solutions on a BRUKER 300 operating 300 MHz for ¹H- and ¹³C-NMR spectroscopy, respectively. Chemical shifts are reported in parts per million (ppm) relative to TMS as internal standards. IR spectra were recorded on a JASCO FT/IR-230 spectrometer.

Preparation of *N*-(2-methoxy-1-naphthoyl)pyrrolidine

N-(2-Methoxy-1-naphthoyl)pyrrolidine **1** used for kinetic resolution was prepared according to the literature.³ 2-Methyl-, 2-ethyl-, and 3-methyl-peperidines **2a-c** were commercially available, and were purified by distillation before use.

Kinetic studies for atropisomerism of **1**

Cryostat apparatus was used for measuring CD spectra at low temperature. The powdered crystals of **1** were dissolved into cooled THF in a cryostat apparatus and the CD spectra were monitored. The rate for enantiomerization was determined on the basis of the attenuation of the CD spectra. The activation parameters were obtained from the Eyring equation and Arrhenius plot. When a single crystal of **1** selected randomly was dissolved in THF at 5°C using a cryostat apparatus, a strong Cotton effect was observed at below 350 nm. The Cotton effect gradually decreased with racemization as a result of the rotation about the naphthalene-C(=O) bond. The half-life was 16.2 minutes when the crystals were dissolved in THF at 15°C, and the value increased upon. The rate of racemization was measured at other temperature and $\Delta H^\ddagger$, $\Delta S^\ddagger$ was calculated on the basis of Arrhenium parameters (Table S1).

Table S1. Kinetic parameters for racemization of amides **1** in THF.

temp (°C)	$t_{1/2}$ (sec)	$\Delta G^\ddagger$ (kcal mol ⁻¹)	$\Delta H^\ddagger$ (kcal mol ⁻¹)	$\Delta S^\ddagger$ (cal mol ⁻¹ K ⁻¹)	$k \times 10^{-4}$
5	2445	21.14	14.12	-25.23	1.418
10	1546	21.27	14.11	-25.29	2.241
15	973	21.39	14.10	-25.30	3.563

Arrhenius parameter E value was 14.68 kcal mol⁻¹.

Typical procedure for the reaction of **1** with racemic amines **2a-c**

To a cooled THF solution containing substituted piperidines **2a-c** with or without additives in a two necked flask, a hexane solution of *n*-BuLi was added dropwise at -80°C under argon atmosphere. After the mixture was stirred for another 0.5 h, the reaction vessel was moved to a bath cooled to -20°C. Then, the powdered chiral crystals of naphthamide **1** were added to the prepared solution of lithium amide. After the reaction mixture was stirred for 5 h at the temperature, water was added to quench the reaction, and was extracted with ether. Ether layer was dried over with anhydrous MgSO₄, evaporated off in vacuo, and the product and starting materials in the residual mixture were separated by chromatography on silica gel.

N-(2-(2-Methyl-1-piperidiny)-1-naphthoyl)pyrrolidine **3a**

IR (cm⁻¹, neat) 1624; ¹H-NMR: (CDCl₃) δ 0.96 (d, J =6.8 Hz, 3H), 1.36-1.89 (m, 9H), 1.95-2.04 (m, 2H), 2.60-2.68 (m, 1H), 2.83-2.93 (m, 1H) 3.25-3.33 (m, 2H), 3.72-3.91 (m, 2H), 7.3-7.5 (m, 3H), 7.6-7.8 (m, 3H), ¹³C-NMR (CDCl₃) δ 17.9, 22.3, 24.8, 26.0, 26.9, 27.2, 34.2, 45.4, 47.1, 54.0, 121.6, 124.4, 124.7, 126.6, 127.7, 128.9, 130.4, 130.6, 130.7, 146.3, 168.7; EI-MS m/z (rel intensity): 322 (M⁺, 33); HRMS (FAB-MS) m/z calcd for C₂₁H₂₆N₂O+H 323.2123, found 323.2104.

N-(2-(2-Ethyl-1-piperidiny)-1-naphthoyl)pyrrolidine **3b**

IR (cm⁻¹, neat) 1620; ¹H-NMR: (CDCl₃) δ 0.77 (t, J =7.5 Hz, 3H) 1.31-1.91 (m, 11H) 1.94-2.03 (m, 2H) 2.70-2.89 (m, 1H) 2.80-2.89 (m, 1H) 3.25-3.35 (m, 2H) 3.45-3.52 (m, 1H) 3.70-3.89 (m, 2H) 7.27-7.30 (d, J =8.9, 1H) 7.34-7.46 (m, 2H) 7.73-7.79 (m, 3H), ¹³C-NMR (CDCl₃) δ 10.9, 21.3, 22.5, 24.7, 25.9, 27.1, 29.6, 45.4, 47.0, 51.2, 60.5, 121.3, 124.3, 124.5, 126.7, 127.7, 128.9, 129.8, 130.1, 130.8, 146.5, 168.8; EI-MS m/z (rel intensity): 336 (M⁺, 12); HRMS (FAB-MS) m/z calcd for C₂₂H₂₈N₂O+H 337.2280, found 337.2286.

***N*-(2-(3-Methyl-1-piperidiny)-1-naphthoyl)pyrrolidine 3c**

This material existed as a mixture of two rotamers. IR (cm⁻¹, neat) 1623; ¹H-NMR: (CDCl₃) δ 0.88-0.90 (d, *J*=6.5 Hz, 3H) 0.97-0.99 (d, *J*=6.6 Hz, 3H) 1.02-1.11 (m, 2H) 1.51-1.90 (m, 14H) 1.92-2.03 (m, 4H) 2.28-2.35 (m, 1H) 2.55-2.63 (m, 1H) 2.69 (t, *J*=10.3 Hz, 10.4 Hz, 1H) 2.80-2.89 (m, 2H) 2.96-3.05 (m, 1H) 3.12-3.16 (m, 2H) 3.23-3.36 (m, 2H) 3.58-3.87 (m, 6H) 7.29-7.31 (d, *J*=9.0 Hz, 2H) 7.36 (t, *J*=7.3 Hz, 7.4 Hz, 2H) 7.44 (t, *J*=7.8 Hz, 7.0 Hz, 2H) 7.77 (t, *J*=8.3 Hz, 8.8 Hz, 6H), ¹³C-NMR (CDCl₃) δ 19.2, 19.5, 24.8, 25.9, 26.4, 26.5, 32.0, 32.3, 32.8, 32.9, 45.5, 47.1, 51.7, 54.9, 59.3, 62.2, 119.5, 124.3, 126.8, 127.7, 128.0, 129.6, 130.0, 130.0, 130.7, 147.1, 168.9; EI-MS *m/z* (rel intensity): 322 (M⁺, 31); HRMS (FAB-MS) *m/z* calcd for C₂₁H₂₆N₂O+H 323.2123, found 323.2104.

Figure S1. ^1H NMR spectrum of 3a

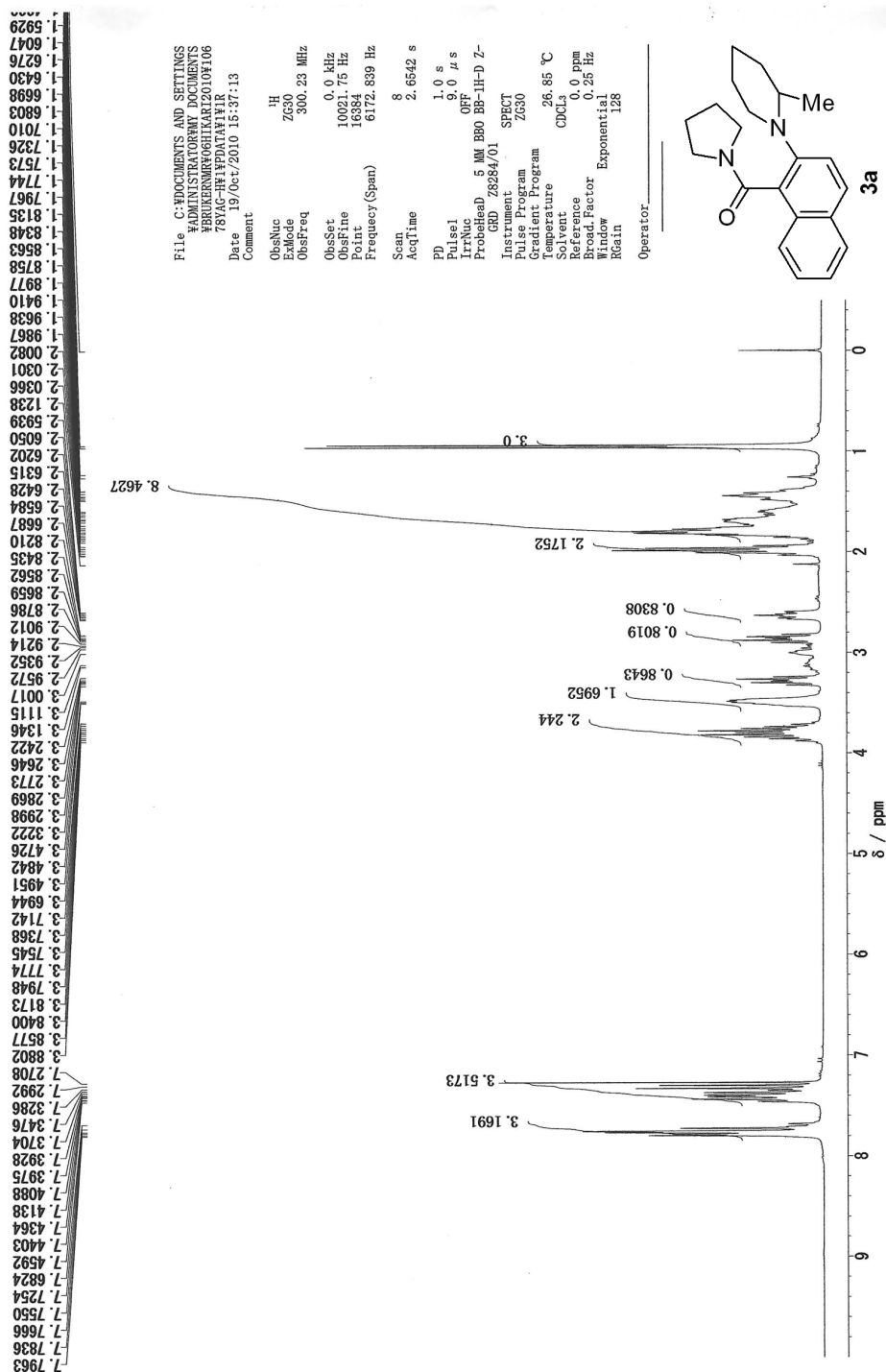


Figure S2. ^{13}C NMR spectrum of 3a

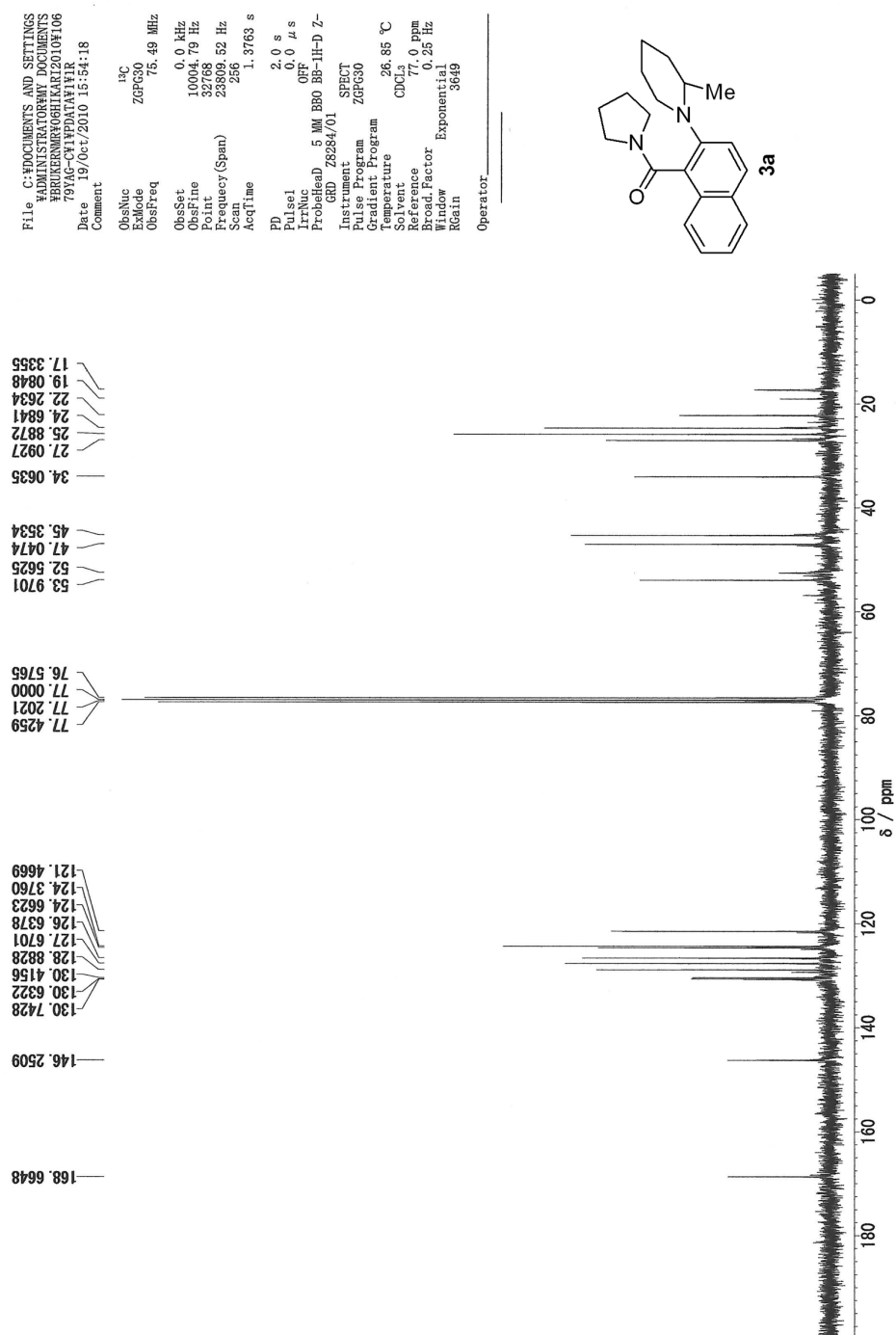
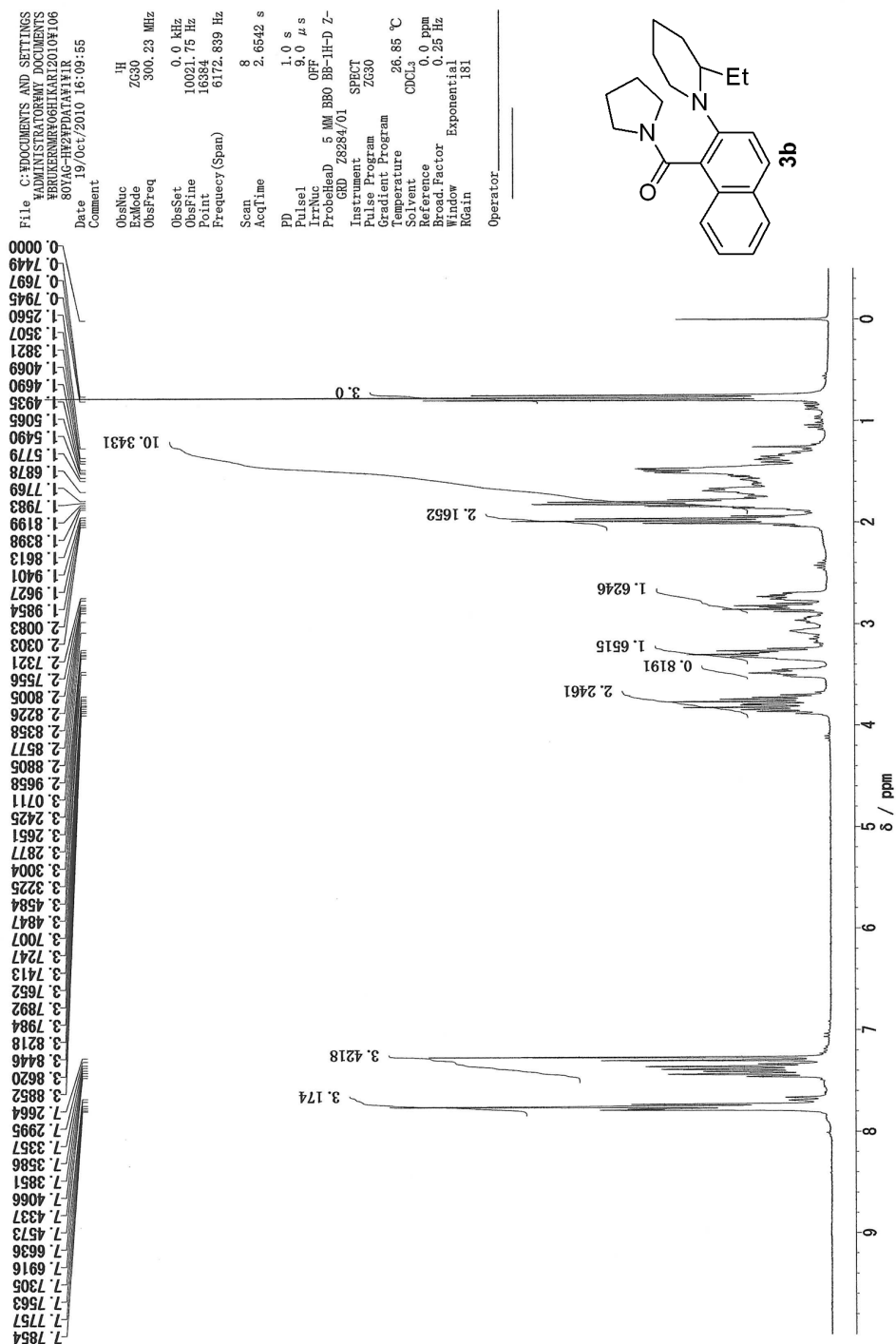


Figure S3. ¹H NMR spectrum of 3b





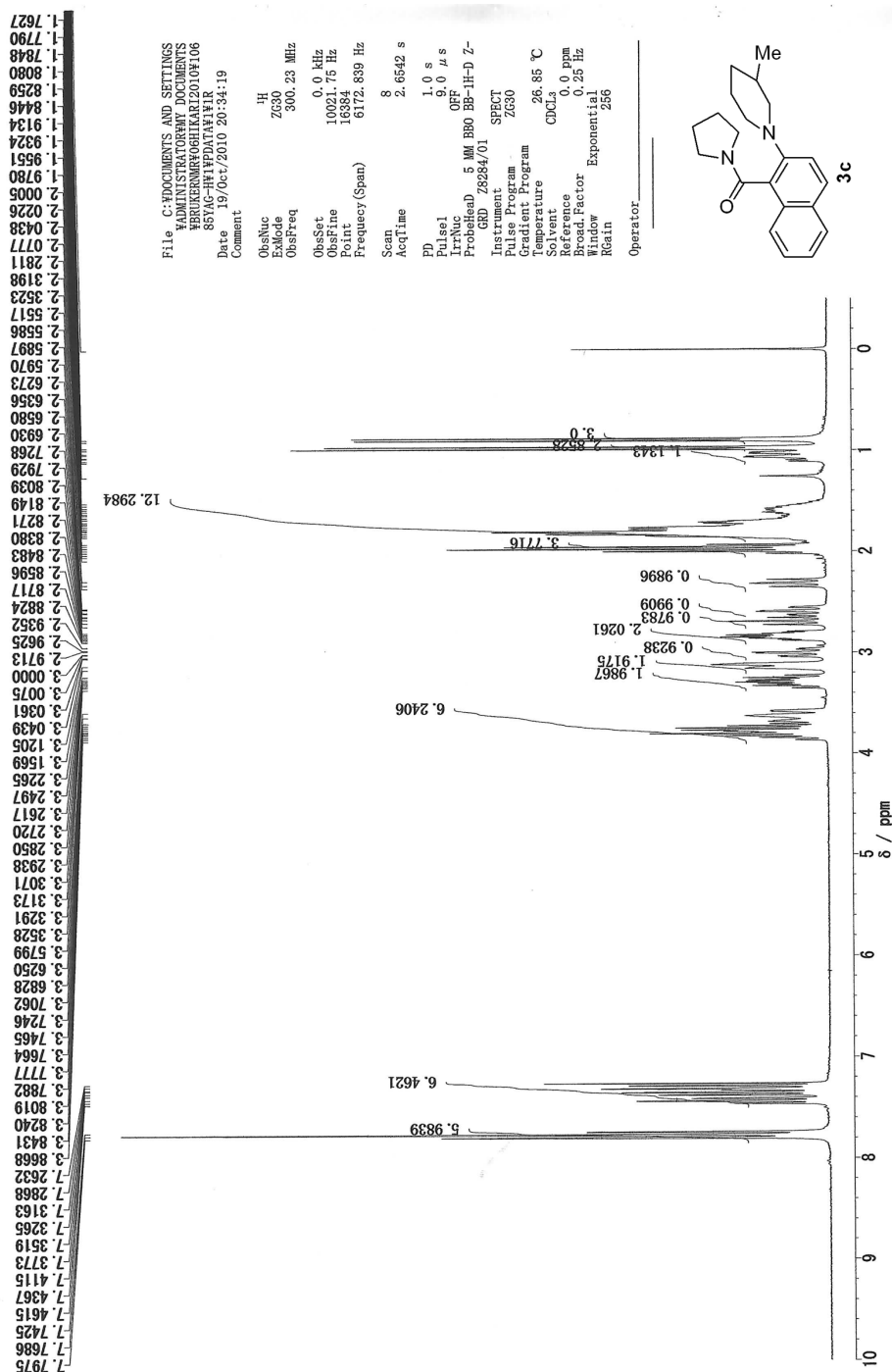


Figure S6. ^{13}C NMR spectrum of **3c**

