Supporting Information for
Synthesis of Carboxamides by LDA-Catalyzed Haller-Bauer and Cannizzaro
Reactions

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General Methods. Infrared (IR) spectra were recorded on a JASCO FT/IR 460 plus spectrometer. ¹H NMR spectra were measured on a Varian Gemini-2000 spectrometer (300 MHz) at ambient temperature. Data were recorded as follows: chemical shift in ppm from internal tetramethylsilane on the δ scale, multiplicity (s = singlet; d = doublet; t = triplet; m = multiplet), coupling constant (Hz), integration, and assignment. ¹³C NMR spectra were measured on Varian Gemini-2000 (75 MHz) spectrometer. Chemical shifts were recorded in ppm from the solvent resonance employed as the internal standard (deuteriochloroform at 77.00 ppm). High-performance liquid chromatography (HPLC) analysis was conducted using Shimadzu LC-10 AD coupled diode array-detector SPD-MA-10A-VP and chiral column of CHIRALCEL OD-H (Daicel chemical industries, LTD.). All experiments were carried out under an atmosphere of dry nitrogen. 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 column chromatography on silica gel (E. Merck Art. 9385). High resolution mass spectral analyses (HRMS) were performed at Chemical Instrument Center, Nagoya University.

In experiments that required dry solvents, tetrahydrofuran (THF), toluene, and diethyl ether were purchased from KANTO CHEMICAL as the “anhydrous”. Organic substrates, were almost commercially available, and were distilled.

General Procedure for the Haller–Bauer Reaction of Benzylic Ketones with Lithium *N*-Alkylamides (Table 2). BuLi (1.58 M in hexane solution, 1.51 mL, 2.4 mmol) was added dropwise

to a solution of amine (2.2 mmol) and *i*-Pr₂NH (28 μ L, 0.2 mmol) in THF (2 mL) at 0 °C under nitrogen atmosphere. After being stirred for 15 min, a solution of ketone (2.0 mmol) in THF (2 mL) was added and the mixture was stirred for 30 min at 0 °C and at room temperature for 5 h. The reaction was then quenched with 1 M HCl (25 mL), the mixture was extracted with AcOEt (3 x 20 mL). The organic layer was dried over Na₂SO₄ and concentrated. The residue was purified by column chromatography on silica gel to yield the corresponding carboxamide.

***N*-Hexyl-6-phenylhexanamide:** ¹H NMR (300 MHz, CDCl₃) δ 0.79–1.00 (m, 3H), 1.10–1.54 (m, 10H), 1.65 (m, 4H), 2.14 (t, *J*=7.8 Hz, 2H), 2.61 (t, *J*=7.8 Hz, 2H), 3.22 (q, *J*=6.9 Hz, 2H), 5.40 (brs, 1H), 7.11–7.40 (m, 5H); ¹³C NMR (75 MHz, CDCl₃) δ 14.0, 22.5, 25.6, 26.5, 28.8, 29.6, 31.1, 31.4, 35.7, 36.7, 39.4, 125.6, 128.2 (2C), 128.3 (2C), 142.5, 172.9; IR (KBr) 3309, 2930, 2853, 1636, 1604, 1539, cm⁻¹; HRMS (EI) calcd for C₁₈H₂₉NO (M⁺) 275.2249, obsd 275.2239.

***N*-Isopropyl-6-phenylhexanamide:** ¹H NMR (300 MHz, CDCl₃) δ 1.12 (d, *J*=6.6 Hz, 6H), 1.31–1.39 (m, 2H), 1.57–1.69 (m, 4H), 2.10 (t, *J*=7.8 Hz, 2H), 2.60 (t, *J*=7.8 Hz, 2H), 3.99–4.14 (m, 1H), 5.36 (brs, 1H), 7.14–7.29 (m, 5H); ¹³C NMR (75 MHz, CDCl₃) δ 22.8 (2C), 25.6, 28.8, 31.1, 35.7, 36.8, 41.1, 125.6, 128.1 (2C), 128.3 (2C), 142.5, 172.0; IR (KBr) 3304, 2933, 2858, 1638, 1606, 1545 cm⁻¹; HRMS (EI) calcd for C₁₅H₂₃NO (M⁺) 233.1780, obsd 233.1770.

***N*-Benzyl-6-phenylhexanamide:** ¹H NMR (300 MHz, CDCl₃) δ 1.38–1.40 (m, 2H), 1.60–1.72 (m, 4H), 2.18 (t, *J*=7.8 Hz, 2H), 2.60 (t, *J*=7.8 Hz, 2H), 4.40 (d, *J*=5.7 Hz, 2H), 5.90 (brs, 1H), 7.10–7.40 (m, 10H); ¹³C NMR (75 MHz, CDCl₃) δ 25.5, 28.8, 31.1, 35.7, 36.6, 43.5, 125.6, 127.4, 127.7 (2C), 128.2 (2C), 128.3 (2C), 128.6 (2C), 138.3, 142.4, 172.8; IR (KBr) 3296, 2928, 2850, 1632, 1604, 1551 cm⁻¹; HRMS (EI) calcd for C₁₉H₂₃NO (M⁺) 281.1780, obsd 281.1801.

***N*-Hexyl-2-phenylacetamide:**¹ ¹H NMR (300 MHz, CDCl₃) δ 0.85 (t, *J*=7.2 Hz, 3H), 1.20–1.23 (m, 6H), 1.40 (t, *J*=7.2 Hz, 2H), 3.19 (q, *J*=7.2 Hz, 2H), 3.58 (s, 2H), 5.32 (brs, 1H), 7.41–7.20 (m, 5H).

***N*-Hexylpropionamide:**² ¹H NMR (300 MHz, CDCl₃) δ 0.89 (t, *J*=4.5 Hz, 3H), 1.16 (m, 3H), 1.29 (m, 6H), 1.49 (t, 2H, 6.6 Hz), 2.20 (q, 2H, 8 Hz), 3.24 (q, 2H, 5.7 Hz), 5.50 (br, 1H).

***N*-Hexylacetamide:**³ ¹H NMR (300 MHz, CDCl₃) δ 0.89 (t, *J*=7.2 Hz, 3H), 1.12–1.29 (m, 9H), 1.49 (t, *J*=7.2 Hz, 2H), 1.98 (s 3H), 2.20 (m, 2H), 3.23 (q, *J*=6.9 Hz, 2H), 5.58 (brs, 1H).

Kinetic Resolution of Racemic 2-Phenylcyclohexanone (1) by the Haller–Bauer Reaction with

(1*R*,2*R*)-Dilithium Diphenylethylenediamide (7) (Table 3). BuLi (633 μ L, 1.0 mmol, 1.58 M in hexane solution) was added dropwise to a solution of (1*R*,2*R*)- diphenylethylenediamine (106 mg, 0.5 mmol) in THF (1 mL) at 0 °C under nitrogen atmosphere. After being stirred for 15 min, **1** (89 mg, 0.5 mmol) in THF (1 mL) was added dropwise and the mixture was stirred for 3 h at 0 °C and at room temperature for 3 h. The reaction was then quenched with aqueous NH₄Cl (25 mL), the mixture was extracted with AcOEt (3 x 20 mL). The organic layer was dried over Na₂SO₄ and concentrated. The residue was purified by column chromatography on silica gel (EtOAc/hexane = 1/2 to 1/1, MeOH/EtOAc = 1/1 as the eluent) to yield **8** (77 mg, 40 % yield) and **1** (30 mg, 35 % yield).

***N*-((1*R*,2*R*)-2'-Amino-1',2'-diphenylethyl)-6-phenylhexanamide (8):** ¹H NMR (300 MHz, CDCl₃) δ 1.24 (m, 2H), 1.41–1.63 (m, 4H), 2.15 (m, 2H), 2.56 (t, *J*=8.1 Hz, 2H), 2.56 (t, 2H, 8.1 Hz), 4.43 (d, *J*=3.0 Hz, 1H), 5.14 (dd, 1H, *J*=3.0, 7.8 Hz, 1H), 6.75 (d, *J*=7.8 Hz, 1H), 7.10–7.48 (m, 15H); ¹³C NMR (75 MHz, CDCl₃) δ 25.5, 28.8 31.2, 35.7, 36.6, 58.2, 59.2, 125.6, 126.36, 126.40, 127.2 (2C), 127.37 (2C), 127.43 (2C), 128.2 (2C), 128.30 (2C), 128.34 (2C), 140.5, 141.9, 142.5, 172.5; IR (KBr); 3438 (br), 2923, 2852, 1640, 1603, 1527, 1496, 1452 cm⁻¹; HRMS (FAB) calcd for C₂₆H₃₀N₂O (M⁺+1) 387.2436, obsd 387.2420.

(*R*)-2-Phenylcyclohexanone (1):⁴ ¹H NMR (300 MHz, CDCl₃) δ 1.82–2.61 (m, 8H), 3.61 (dd, *J*=5.4, 11.7 Hz, 1H), 7.12– $\tilde{\square}\square\square$ (m, 5H); HPLC (Daicel OD-H column, hexane:*i*-PrOH = 100:1, flow rate 1 mL/min) *t*_R=13.2 ((*S*)-(-)-enantiomer), 14.8 ((*R*)-(+)-enantiomer) min; [α]_D²⁰ = 67 (*c* = 1.01, CHCl₃) for 66% ee of the product.

General Procedure for the Cannizzaro-type Reaction of Aldehydes with Lithium *N*-Alkylamides or Lithium *N,N*-Dialkylamides (Tables 4 and 5).

Method A. NaH (40 mg, 1.0 mmol (60% dispersion in mineral oil)) was added to a solution of amine (1.1 mmol) in THF (2 mL) at 0 °C under nitrogen atmosphere. After being stirred for 30 min, aldehyde (2.0 mmol) in THF (2 mL) was added and the mixture was stirred for 30 min at 0 °C and at room temperature for 5 h. The reaction was then quenched with 1 M HCl (25 mL), the mixture was extracted with AcOEt (3 x 20 mL). The organic layer was dried over Na₂SO₄ and concentrated. The residue was purified by column chromatography on silica gel to yield amide and alcohol.

Method B. BuLi (759 μ L, 1.2 mmol, a 1.58 M solution in hexane) was added dropwise to a solution of amine (1.1 mmol) and *i*-Pr₂NH (14 μ L, 0.1 mmol) in THF (2 mL) at 0 °C under nitrogen atmosphere. After being stirred for 30 min, aldehyde (2.0 mmol) in THF (2 mL) was added and the mixture was stirred for 30 min at 0 °C and at 40 °C for a further 5 h. The reaction was then quenched with 1 M HCl (25 mL), the mixture was extracted with AcOEt (3 x 20 mL). The organic layer was dried over Na₂SO₄ and concentrated. The residue was purified by column chromatography on silica gel to yield amide and alcohol.

***N*-Hexylbenzamide:**⁵ ¹H NMR (300 MHz, CDCl₃) δ 0.90 (t, *J*=6.9 Hz, 3H), 1.31–1.64 (m, 8H), 3.46 (m, 2H), 6.21 (br, 1H), 7.41 (m, 3H), 7.77 (m, 2H).

***N*-Hexyl-4-methoxybenzamide:** ¹H NMR (300 MHz, CDCl₃) δ 7.73 (d, 2H, 8.7 Hz), 6.91 (d, 2H, 8.7 Hz), 0.89 (t, *J*=7.2 Hz, 3H), 1.19–1.41 (m, 6H), 1.50–1.61 (m, 2H), 3.43 (q, *J*=7.2 Hz, 2H), 3.85 (s, 3H), 6.10 (brs, 1H). This compound is commercially available.

***N*-Hexyl-4-trifluoromethylbenzamide:** ¹H NMR (300 MHz, CDCl₃) δ 0.9 (t, *J*=7.2 Hz, 3H), 1.32–1.38 (m, 6H), 1.58–1.65 (m, 2H), 3.47 (q, *J*=6.3 Hz, 2H), 6.11 (brs, 1H), 7.70 (d, *J*=8.1 Hz, 2H), 7.87 (d, *J*=8.1 Hz, 2H); ¹³C NMR (75 MHz, CDCl₃) δ 14.0, 22.5, 26.6, 29.5, 31.4, 40.3, 125.5, 125.6, 126.8, 127.3 (2C), 134.2 (q, *J*=574 Hz, 1C, CF₃), 166.3; IR (KBr) 3311, 2930, 2857, 1701, 1641, 1620, 1552 cm⁻¹; HRMS (EI) calcd for C₁₄H₁₈F₃NO (M⁺) 273.1340, obsd 273.1331.

***N*-Hexylisobutyramide:**⁶ ¹H NMR (300 MHz, CDCl₃) δ 0.88 (t, *J*=6.9 Hz, 3H), 1.15 (d, *J*=6.6 Hz, 6H), 1.29 (m, 6H), 1.49 (m, 2H), 2.33 (s, 1H), 3.24 (q, *J*=6.3 Hz, 2H), 5.41 (brs, 1H).

***N*-Hexyl-2,2-dimethylpropionamide:**⁶ ¹H NMR (300 MHz, CDCl₃) δ 0.88 (t, 3H, *J*=5.7 Hz, 3H), 1.19 (s, 6H), 1.29 (m, 8H), 1.49 (t, *J*=7.5 Hz, 2H), 3.23 (m, 2H), 5.61 (brs, 1H).

1-Benzoylpyrrolidine:⁷ ¹H NMR (300 MHz, CDCl₃) δ 1.84–2.06 (m, 4H), 3.42 (t, *J*=6.6 Hz, 2H), 3.64 (t, *J*=6.9 Hz, 2H), 7.35–7.40 (m, 3H), 7.47–7.53 (m, 2H).

1-Benzoylpiperidine:⁸ ¹H NMR (300 MHz, CDCl₃) δ 1.52 (br, 2H), 1.68 (brs, 4H), 3.34 (brs, 2H), 3.72 (brs, 2H), 7.39 (brs, 5H).

***N,N*-Diethylbenzamide:**⁹ ¹H NMR (300 MHz, CDCl₃) δ 1.11 (brs, 3H), 1.25 (brs, 3H), 3.25 (brs, 2H), 3.55 (brs, 2H), 7.32–7.39 (m, 5H).

Benzamide: ¹H NMR (300 MHz, CDCl₃) δ 7.10–7.50 (m, 3H), 7.78–8.09 (m, 2H). This compound is commercially available.

***N*-Phenylbenzamide:**¹⁰ ¹H NMR (300 MHz, CDCl₃) δ 7.14–7.89 (m, 10H); ¹³C NMR (75 MHz,

CDCl₃) δ 120.1, 124.6, 126.9, 128.5, 129.0, 131.5, 135.2, 138.1, 165.8; This compound is commercially available.

Benzyl Alcohol: ¹H NMR (300 MHz, CDCl₃) δ 4.70 (s, 2H), 7.31-7.50 (m, 5H). This compound is commercially available.

(4-Methoxyphenyl)methanol: ¹H NMR (300 MHz, CDCl₃) δ 3.81 (s, 3H), 4.61 (s, 2H), 6.89 (d, $J=8.0$ Hz, 2H), 7.29 (d, $J=8.0$ Hz, 2H). This compound is commercially available.

(4-Trifluoromethylphenyl)methanol: ¹H NMR (300 MHz, CDCl₃) δ 2.81 (t, $J=6.0$ Hz, 1H), 4.68 (d, $J=6.0$ Hz, 2H), 7.40 (s, $J=8.0$ Hz, 2H), 7.57 (d, $J=8.0$ Hz, 2H). This compound is commercially available.

Preparation of a 0.4 M Solution of Anhydrous Phenylglyoxal in Toluene. A 20-mL, single-necked, pear-shaped-flask equipped with a Teflon-coated magnetic stirring bar and a Dean–Stark apparatus surmounted by a reflux condenser was charged with phenylglyoxal (304 mg, 2 mmol) and toluene (5 mL). The mixture was brought to be heated at azeotropic reflux with removal of water. After being stirred for 1 h, the resulting mixture was cooled to ambient temperature. ¹H NMR (300 MHz, toluene-*d*₆) δ 7.95–7.98 (m, 2H), 9.03 (s, 1H).

Procedure for the Haller–Bauer Reaction of Phenylglyoxal with Sodium Pyrrolidine (Table 8).

Pyrrolidine (92 μ L, 1.1 mmol) was added dropwise to a suspension of NaH (44 mg, 1.1 mmol (60% dispersion in mineral oil)) in THF (2 mL) at 0 °C under nitrogen atmosphere. After being stirred for 30 min, anhydrous phenylglyoxal (a 0.4 M in toluene solution, 1.0 mmol) was added and the mixture was stirred for 30 min at 0 °C and at room temperature for 5 h. The reaction was then quenched with 1 M HCl (25 mL), the mixture was extracted with AcOEt (3 x 20 mL). The organic layer was dried over Na₂SO₄ and concentrated. The residue was purified by column chromatography on silica gel to yield 1-(2'-hydroxy-2'-phenylacetyl)pyrrolidine¹¹ (85% yield). ¹H NMR (300 MHz, CDCl₃) δ 1.71–1.91 (m, 4H), 2.81–2.87 (m, 1H), 3.35–3.63 (m, 3H), 4.80 (br, 1H), 5.05 (s, 1H), 7.23–7.41 (m, 5H).

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