Alkylation of Magnesium Enamide with Alkyl Chlorides and Fluorides

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General. All the reactions dealing with air- or moisture- sensitive compounds were carried out in a dry reaction vessel under positive pressure of argon or nitrogen. Air- and moisture-sensitive liquids and solutions were transferred via a syringe or a stainless steel cannula. Analytical thin-layer chromatography was performed on a glass plates coated with 0.25 mm 230–400 mesh silica gel containing a fluorescent indicator (Merck, #1.05715.0009). Thin layer chromatography plates were visualized by exposure to ultraviolet light (254 nm) and/or by immersion in an acidic staining solution of *p*-anisaldehyde followed by heating on a hot plate. Organic solutions were concentrated by rotary evaporation at *c.a.* 30 mmHg. Flash column chromatography was performed on Kanto Silica gel 60 (spherical, neutral, 140–325 mesh) as described by Still et al.¹

Instrumentation. Proton nuclear magnetic resonance (¹H NMR) and carbon nuclear magnetic resonance (¹³C NMR) spectra were recorded on JEOL AL-400 (400 MHz), JEOL ECX-400 (400 MHz) or JEOL ECA-500 (500 MHz) NMR spectrometers. Chemical shift values of proton are reported in parts per million (ppm, δ scale) downfield from tetramethylsilane and are referenced to residual proton of CDCl₃ (δ 7.26). Carbon nuclear magnetic resonance spectra (¹³C NMR) were recorded at 125 or 100 MHz: chemical shifts for carbons are reported in parts per million (ppm, δ scale) downfield from tetramethylsilane and are referenced to the carbon resonance of CDCl₃ (δ 77.0). Data are presented as: chemical shift, multiplicity (s = singlet, d = doublet, t = triplet, q = quartet, quint = quintet, sext = sextet, sept = septet, m = multiplet and/or multiplet resonances, br = broad),

(1) Still, W. C.; Klahn, M.; Mitra, A. *J. Org. Chem.* **1978**, *43*, 2923–2924.

coupling constant in hertz (Hz), and signal area integration in natural numbers, assignment (*italic*). IR spectra recorded on a FT/IR-420 (JASCO) or a React IR 1000 Reaction Analysis System equipped with DuraSample IR (ASI Applied System) are reported in cm^{-1} . Characteristic IR absorptions are reported in cm^{-1} . High-resolution mass spectra are taken with EI (electron impact) method at a JEOL GC-mate II, APCI (atmosphere pressure chemical ionization) or ESI (electron spray ionization) method at a JEOL JMS-T100LC.

Solvent. Anhydrous tetrahydrofuran (THF) was purchased from Kanto Chemical Co. and dried over aluminum columns². Water content of the solvent was determined with a Karl-Fischer Moisture Titrator (MKC-210, Kyoto Electronics Company) to be less than 10 ppm.

Materials. Materials were purchased from Tokyo Kasei Kogyo Co., Aldrich Inc., and other commercial suppliers, and were used after appropriate purification unless otherwise noted. Florisil[®] (100–200 mesh) was purchased from Yoneyama Yakuhin Kogyo Co., Ltd. Mesitylmagnesium bromide (MesMgBr) was prepared from bromomesitylene and magnesium (turnings) using a standard method and titrated before use. Imine substrates were prepared according to the procedure described below. Because of their hygroscopic nature, the imine substrates were not subjected to precise elemental analysis, and hence, were kept and handled under an inert atmosphere after distillation.

GC and HPLC Analyses. Diastereoselectivity (*ds*) and yield (by using octane, decane, or undecane as an internal standard) were determined for a crude product by GC analyses on a Shimadzu GC-14B instrument equipped with an FID detector and a capillary column, HR-1 (Shinwa, 25 m $\times$ 0.25 mm i.d., 0.25 mm film thickness). Enantioselectivity was determined by GC analyses on a Shimadzu GC-14B instrument equipped with an FID detector and a capillary column, γ -DEX 225 (Supelco, 30 m $\times$ 0.25 mm i.d., 0.25 mm film), or by HPLC analyses on a JASCO CD-2095 Plus equipped with chiral column, CHIRALCEL OJ-H (Daicel, 4.6 $\times$ 250 mm).

Preparation of *N'*-(1-Ethylpropylidene)-*N,N*-dimethyl-1,2-ethanediamine

(2) Pangborn, A. B.; Giardello, M. A.; Grubbs, R. H.; Rosen, R. K.; Timmers, F. J. *Organometallics* **1996**, *15*, 1518–1520.

Molecular sieves (4A, 12 g, dry) were added to 3-pentanone (8.61 g, 100 mmol) and *N,N*-dimethylaminoethylimine (8.85 g, 100 mmol). The reaction mixture was heated to 80 °C for 1 d. The reaction mixture was cooled to ambient temperature and then molecular sieves were filtered with a pad of celite and washed with dry Et₂O (20 mL, five times). The filtrate was evaporated *in vacuo* and distilled to yield 15.1 g (90% yield) of the imine as a colorless liquid. Bp 75 °C/6 mmHg; IR (neat) 2972, 2937, 2818, 2768, 1660 (C=N), 1459, 1374, 1266, 1173, 1150, 1042, 932, 861, 784; ¹H NMR (500 MHz, CDCl₃) δ 1.07 (q, *J* = 7.4 Hz, 6H, C(CH₂CH₃)₂), 2.22–2.32 (m, 4H, C(CH₂CH₃)₂), 2.29 (s, 3H, N(CH₃)₂), 2.56 (t, *J* = 7.5 Hz, 2H, (CH₃)₂NCH₂CH₂), 3.43 (t, *J* = 7.5 Hz, 2H, (CH₃)₂NCH₂CH₂); ¹³C NMR (125 MHz, CDCl₃) δ 10.8, 11.0, 23.9, 32.7, 45.9 (2C), 49.1, 60.6, 176.1.

***N'*-(1-Ethylpropylidene)-*N,N*-diethyl-1,2-ethanediamine**

Bp 85 °C/5 mmHg; IR (neat) 2968, 2934, 2896, 2802, 1660 (C=N), 1463, 1378, 1293, 1204, 1166, 1069, 938, 799, 741; ¹H NMR (500 MHz, CDCl₃) δ 1.02–1.12 (m, 12H, N(CH₂CH₃)₂, C(CH₂CH₃)₂), 2.20–2.31 (m, 4H, C(CH₂CH₃)₂), 2.60 (q, *J* = 7 Hz, 4H, N(CH₂CH₃)₂), 2.70 (t, *J* = 8.0 Hz, 2H, Et₂NCH₂CH₂), 3.43 (t, *J* = 8.0 Hz, 2H, Et₂NCH₂CH₂); ¹³C NMR (125 MHz, CDCl₃) δ 10.8, 11.0, 11.8 (2C), 23.9, 32.7, 47.5 (2C), 49.2, 54.0, 176.0.

(1-Ethylpropylidene)-(2-pyrrolidin-1-ylethyl)amine

Bp 85 °C/2.8 mmHg; IR (neat) 2968, 2934, 2783, 1660 (C=N), 1459, 1351, 1293, 1150, 1038, 880; ¹H NMR (500 MHz, CDCl₃) δ 1.06 (q, *J* = 8.6 Hz, 6H, C(CH₂CH₃)₂), 1.75–1.84 (m, 4H, CH₂CH₂CH₂CH₂), 2.20–2.31 (m, 4H, CH₂CH₃), 2.54–2.63 (m, 4H, CH₂CH₂CH₂CH₂), 2.73 (t, *J* = 7.9 Hz, 2H, CH₂CH₂N=C), 3.48 (t, *J* = 7.9 Hz, 2H, CH₂N=C); ¹³C NMR (125 MHz, CDCl₃) δ 10.8, 11.0, 23.3 (2C), 23.9, 32.6, 50.2, 54.5 (2C), 57.4, 176.0.

(1-Ethylpropylidene)-(2-piperidin-1-ylethyl)amine

Bp 82 °C/1.3 mmHg; IR (neat) 2968, 2934, 2856, 2802, 1660 (C=N), 1455, 1305, 1158, 1123, 1038; ^1H NMR (500 MHz, CDCl_3) δ 1.06 (q, J = 8.4 Hz, $\text{C}(\text{CH}_2\text{CH}_3)_2$), 1.39–1.49 (m, 2H, $\text{CH}_2\text{CH}_2\text{CH}_2\text{CH}_2\text{CH}_2$), 1.54–1.63 (m, 4H, $\text{CH}_2\text{CH}_2\text{CH}_2\text{CH}_2\text{CH}_2$), 2.20–2.29 (m, 4H, $\text{C}(\text{CH}_2\text{CH}_3)_2$), 2.40–2.55 (m, 4H, $\text{CH}_2\text{CH}_2\text{CH}_2\text{CH}_2\text{CH}_2$), 2.59 (t, J = 7.9 Hz, 2H, $\text{CH}_2\text{CH}_2\text{N}=\text{C}$), 3.47 (t, J = 7.9 Hz, 2H, $\text{CH}_2\text{N}=\text{C}$); ^{13}C NMR (125 MHz, CDCl_3) δ 10.8, 11.1, 23.9, 24.3, 25.9 (2C), 32.7, 48.5, 55.0 (2C), 62.1, 176.0.

(1-Ethylpropylidene)-(2-morpholin-4-ylethyl)amine

Bp 95 °C/2.4 mmHg; IR (neat) 2968, 2937, 2853, 2810, 1660 (C=N), 1455, 1301, 1139, 1116, 1007, 915, 869; ^1H NMR (500 MHz, CDCl_3) δ 1.06 (q, J = 7.5 Hz, 6H, $\text{C}(\text{CH}_2\text{CH}_3)_2$), 2.19–2.30 (m, 2H, $\text{C}(\text{CH}_2\text{CH}_3)_2$), 2.48–2.58 (m, 4H, $\text{N}(\text{CH}_2\text{CH}_2)_2\text{O}$), 2.64 (t, J = 7.4 Hz, 2H, $\text{CH}_2\text{CH}_2\text{N}=\text{C}$), 3.47 (t, J = 7.4 Hz, 2H, $\text{CH}_2\text{N}=\text{C}$), 3.67–3.76 (m, 4H, $\text{N}(\text{CH}_2\text{CH}_2)_2\text{O}$); ^{13}C NMR (125 MHz, CDCl_3) δ 10.8, 11.1, 23.9, 32.6, 48.1, 54.1 (2C), 59.9, 66.9 (2C), 176.2.

***N'*-(1-Propylbutylidene)-*N,N*-diethyl-1,2-ethanediamine**

Bp 96 °C/2.5 mmHg; IR (neat) 2964, 2934, 2872, 2802, 1660 (C=N), 1463, 1382, 1293, 1204, 1069;

^1H NMR (500 MHz, CDCl_3) δ 0.88–1.08 (m, 12H, $\text{N}(\text{CH}_2\text{CH}_3)_2$, $\text{C}(\text{CH}_2\text{CH}_2\text{CH}_3)_2$), 1.47–1.58 (m, 4H, $\text{C}(\text{CH}_2\text{CH}_2\text{CH}_3)_2$), 2.14–2.24 (m, 4H, $\text{C}(\text{CH}_2\text{CH}_2\text{CH}_3)_2$), 2.60 (q, $J = 7.2$ Hz, 4H, $\text{N}(\text{CH}_2\text{CH}_3)_2$), 2.69 (t, $J = 8.0$ Hz, 2H, $\text{Et}_2\text{NCH}_2\text{CH}_2$), 3.43 (t, $J = 8.0$ Hz, 2H, $\text{Et}_2\text{NCH}_2\text{CH}_2$); ^{13}C NMR (125 MHz, CDCl_3) δ 11.8 (2C), 14.0, 14.4, 19.8, 20.2, 33.1, 42.3, 47.5 (2C), 49.4, 54.1, 174.1.

***N'*-Cyclohexylidene-*N,N*-diethyl-1,2-ethanediamine**

Bp 103 °C/6 mmHg; IR (neat) 2968, 2930, 2860, 2806, 1660 (C=N), 1447, 1382, 1343, 1293, 1204, 1069, 772, 741; ^1H NMR (500 MHz, CDCl_3) δ 1.04 (t, $J = 7.2$ Hz, 6H, $\text{N}(\text{CH}_2\text{CH}_3)_2$), 1.60–1.75 (m, 6H, $\text{CH}_2(\text{CH}_2)_3\text{CH}_2$), 2.24–2.34 (m, 4H, $\text{CH}_2(\text{CH}_2)_3\text{CH}_2$), 2.58 (q, $J = 7.2$ Hz, 4H, $\text{N}(\text{CH}_2\text{CH}_3)_2$), 2.69 (t, $J = 7.2$ Hz, 2H, $\text{Et}_2\text{NCH}_2\text{CH}_2$), 3.41 (t, $J = 7.2$ Hz, 2H, $\text{Et}_2\text{NCH}_2\text{CH}_2$); ^{13}C NMR (125 MHz, CDCl_3) δ 11.8 (2C), 26.0, 26.9, 27.6, 29.0, 39.9, 47.5 (2C), 48.7, 53.9, 173.6.

***N'*-(1-Isopropylpropylidene)-*N,N*-diethyl-1,2-ethanediamine**

Bp 79 °C/2.0 mmHg; *E:Z* = 79:21; IR (neat) 2968, 2934, 2876, 2806, 1660 (C=N), 1467, 1382, 1293, 1204, 1069. *E*-isomer: ^1H NMR (500 MHz, CDCl_3) δ 0.98–1.12 (m, 15H, CCH_2CH_3 , $\text{CH}(\text{CH}_3)_2$), $\text{N}(\text{CH}_2\text{CH}_3)_2$), 2.19–2.28 (m, 2H, CCH_2CH_3), 2.44–2.56 (m, 1H, $\text{CCH}(\text{CH}_3)_2$), 2.60 (q, $J = 7.1$ Hz, 4H, $\text{N}(\text{CH}_2\text{CH}_3)_2$), 2.70 (t, $J = 7.7$ Hz, 2H, $\text{Et}_2\text{NCH}_2\text{CH}_2$), 3.45 (t, $J = 7.7$ Hz, 2H, $\text{Et}_2\text{NCH}_2\text{CH}_2$); ^{13}C NMR (125 MHz, CDCl_3) δ 11.3, 11.7 (2C), 20.2 (2C), 22.3, 38.1, 47.5 (2C), 49.2, 54.0, 178.7.

***N'*-(1-Phenylethylidene)-*N,N*-diethyl-1,2-ethanediamine**

Bp 120 °C/3 mmHg; *E*:*Z* = 87:13; IR (neat) 3061 (aromatic C–H), 2968, 2934, 2872, 2802, 1633 (C=N), 1447, 1370, 1282, 1204, 1085, 760, 691.

E-isomer: ^1H NMR (500 MHz, CDCl_3) δ 1.08 (t, $J = 7.2$ Hz, 6H, CH_2CH_3), 2.25 (s, 3H, CCH_3), 2.64 (q, $J = 7.2$ Hz, 4H, CH_2CH_3), 2.73 (t, $J = 7.7$ Hz, 2H, $\text{Et}_2\text{NCH}_2\text{CH}_2$), 3.61 (t, $J = 7.7$ Hz, 2H, $\text{Et}_2\text{NCH}_2\text{CH}_2$), 7.33–7.40 (m, 3H, $\text{CH}(\text{CH})_3\text{CH}$), 7.73–7.79 (m, 2H, $\text{CH}(\text{CH})_3\text{CH}$); ^{13}C NMR (125 MHz, CDCl_3) δ 11.8 (2C), 15.6, 47.5 (2C), 51.0, 53.6, 126.4 (2C), 128.1 (2C), 129.3, 131.7, 165.6.

Z-isomer: ^1H NMR (500 MHz, CDCl_3) δ 0.95 (t, $J = 7.2$ Hz, 6H, CH_2CH_3), 2.29 (s, 3H, CCH_3), 2.46 (q, $J = 7.2$ Hz, 4H, CH_2CH_3), 2.67 (t, $J = 7.7$ Hz, 2H, $\text{Et}_2\text{NCH}_2\text{CH}_2$), 3.32 (t, $J = 7.7$ Hz, 2H, $\text{Et}_2\text{NCH}_2\text{CH}_2$), 7.13 (d, 2H, $\text{CH}(\text{CH})_3\text{CH}$), 7.30–7.41 (m, 3H, $\text{CH}(\text{CH})_3\text{CH}$); ^{13}C NMR (125 MHz, CDCl_3) δ 11.6 (2C), 29.1, 47.3 (2C), 51.3, 51.6, 125.8 (2C), 128.0, 128.4 (2C), 140.0, 169.5.

***N'*-(1-Phenylpropylidene)-*N,N*-diethyl-1,2-ethanediamine**

Bp 130–132 °C/2.8 mmHg; *E*:*Z* = 52:48; IR (neat) 3061 (aromatic C–H), 2968, 2934, 2870, 2802, 1633 (C=N), 1447, 1378, 1289, 1204, 1065, 772, 694.

E-isomer: ^1H NMR (500 MHz, CDCl_3) δ 1.08 (t, $J = 7.2$ Hz, 6H, $\text{N}(\text{CH}_2\text{CH}_3)_2$), 1.11 (t, $J = 7.2$ Hz, 3H, CCH_2CH_3), 2.64 (q, $J = 7.4$ Hz, 4H, $\text{N}(\text{CH}_2\text{CH}_3)_2$), 2.71 (q, $J = 7.8$ Hz, 2H, CCH_2CH_3), 2.86 (t, $J = 7.7$ Hz, 2H, $\text{Et}_2\text{NCH}_2\text{CH}_2$), 3.66 (t, $J = 7.7$ Hz, 2H, $\text{Et}_2\text{NCH}_2\text{CH}_2$), 7.33–7.40 (m, 3H, $\text{CH}(\text{CH})_3\text{CH}$), 7.72–7.78 (m, 2H, $\text{CH}(\text{CH})_3\text{CH}$); ^{13}C NMR (125 MHz, CDCl_3) δ 11.4, 11.7 (2C), 21.9, 47.2 (2C), 50.0, 53.8, 126.6 (2C), 128.0 (2C), 129.1, 139.7, 170.2.

Z-isomer: ^1H NMR (500 MHz, CDCl_3) δ 0.94 (t, $J = 7.2$ Hz, 6H, $\text{N}(\text{CH}_2\text{CH}_3)_2$), 1.06 (t, $J = 7.2$ Hz, 3H, CCH_2CH_3), 2.45 (q, $J = 7.1$ Hz, 4H, $\text{N}(\text{CH}_2\text{CH}_3)_2$), 2.52 (q, $J = 7.4$ Hz, 2H, CCH_2CH_3), 2.66 (q, $J = 7.7$ Hz, 2H, $\text{Et}_2\text{NCH}_2\text{CH}_2$), 3.31 (t, $J = 7.7$ Hz, 2H, $\text{Et}_2\text{NCH}_2\text{CH}_2$), 7.09 (d, $J = 6.9$ Hz, 2H,

$\text{CH}(\text{CH}_3)_2\text{CH}$), 7.27–7.40 (m, 3H, $\text{CH}(\text{CH}_3)_2\text{CH}$); ^{13}C NMR (125 MHz, CDCl_3) δ 10.7, 11.6 (2C), 35.0, 47.4 (2C), 51.1, 53.4, 126.1 (2C), 128.2 (2C), 129.1, 138.4, 173.6.

A typical procedure (Procedure A) for the reaction shown in Table 1; Preparation of 2-cycloheptylpentan-3-one (2)

N' -(1-Ethylpropylidene)- N,N -diethyl-1,2-ethanediamine (0.184 g, 1.0 mmol) was added to mesitylmagnesium bromide (MesMgBr, 0.95 M in THF, 1.16 mL, 1.1 mmol) at room temperature. The reaction mixture was stirred at 80 °C for 1 h. After the solvents were removed *in vacuo*, chlorocycloheptane (0.159 g, 1.2 mmol) was added at room temperature. The reaction was carried out at 45 °C for 24 h and then 60 °C for 12 h. AcOH in H_2O (50 wt%, 1.0 mL) was added slowly at 0 °C. The reaction mixture was stirred at 50 °C for 1 h then cooled to room temperature. The reaction mixture was neutralized with saturated NaHCO_3 aqueous solution. The aqueous layer was extracted with Et_2O five times. The combined organic extracts were dried with Na_2SO_4 . Gas chromatography analysis was carried out (88% yield) by using octane as an internal standard. After the solvent was removed *in vacuo*, the crude product was purified by chromatography on silica gel (10 g, pentane and then 2% Et_2O in pentane) to obtain the title compound (0.157 g, 86% yield) as a colorless liquid.; R_f = 0.38 (10% Et_2O in pentane); IR (neat) 2976, 2922, 2856, 1710 (C=O), 1459, 1378, 1104, 1019, 973, 803; ^1H NMR δ 1.00 (d, J = 6.9 Hz, 3H, CHCH_3), 1.04 (t, J = 7.2 Hz, 3H, CH_2CH_3), 1.13–1.33 (m, 2H, $\text{CHH}(\text{CH}_2)_4\text{CHH}$), 1.35–1.70 (m, 10H, $\text{CHH}(\text{CH}_2)_4\text{CHH}$), 1.79–1.88 (m, 1H, CHCHCH_3), 2.42–2.47 (m, 3H, CHCH_3 , CH_2CH_3); ^{13}C NMR δ 7.8, 12.7, 26.6, 26.9, 28.1, 28.2, 30.0, 33.4, 34.7, 41.2, 52.4, 215.5. Anal. calcd for $\text{C}_{12}\text{H}_{22}\text{O}$ C, 79.06; H, 12.16. found C, 78.92; H, 11.92.

A typical procedure (Procedure B) for the reaction shown in Table 2: Preparation of 5-ethylpentadecan-4-one (9)

N' -(1-Propylbutylidene)- N,N -diethyl-1,2-ethanediamine (0.212 g, 1.0 mmol) was added to mesitylmagnesium bromide (MesMgBr, 0.95 M in THF, 1.16 mL, 1.1 mmol) at room temperature. After stirring at 80 °C for 1 h, 1-fluorodecane (0.192 g, 1.2 mmol) was added at room temperature. The reaction was carried out at 65 °C for 36 h. AcOH in H_2O (50 wt%, 1.0 mL) was added slowly at 0

°C. The reaction mixture was stirred at 50 °C for 1 h then cooled to room temperature. The reaction mixture was neutralized with saturated NaHCO₃ aqueous solution. The aqueous layer was extracted with Et₂O five times. The combined organic extracts were dried with Na₂SO₄. After the solvent was removed *in vacuo*, the crude product was purified by chromatography on silica gel (10 g, pentane and then 2% Et₂O in pentane) to obtain the title compound (0.248 g, 97% yield) as a colorless liquid.; R_f = 0.62 (10% Et₂O in pentane); IR (neat) 2961, 2926, 2856, 1710 (C=O), 1459, 1378, 1123, 1031, 722; ¹H NMR δ 0.82–0.93 (m, 9H, C(CH₂)₂CH₃, CHCH₂CH₃, (CH₂)₉CH₃), 1.15–1.32 (m, 16H, (CH₂)₈), 1.30–1.65 (m, 6H, CCH₂CH₂, CHCH₂CH₃, CHCH₂CH₂), 2.33–2.42 (m, 3H, CH₂C(=O)CH); ¹³C NMR δ 11.9, 13.8, 14.1, 16.9, 22.7, 24.6, 27.5, 29.3, 29.4, 29.6 (2C), 29.8, 31.4, 31.9, 44.2, 53.9, 215.0. Anal. calcd for C₁₇H₃₄O C, 80.24; H, 13.47. found C, 80.16; H, 13.21.

2-Decylcyclohexanone (10)³

The reaction was carried out according to procedure B on a 1.0-mmol scale by using the corresponding imine (0.196 g, 1.0 mmol) and 1-fluorodecane (0.192 g, 1.2 mmol). Conditions; 65 °C, 36 h. The title compound (0.178 g, 75% yield) was obtained as a colorless liquid after silica gel column chromatography.

2,4-Dimethyl-3-tetradodecanone (11) and 4,4-dimethyl-3-tetradodecanone (12)

The reaction was carried out according to procedure B on a 1.0-mmol scale by using the corresponding imine (0.198 g, 1.0 mmol) and 1-fluorodecane (0.192 g, 1.2 mmol). Conditions; 65 °C, 36 h. The title compound (0.216 g, 90% yield, 91:9 mixture determined by ¹H NMR analysis) was obtained as a colorless liquid after silica gel column chromatography. R_f = 0.31 (3% Et₂O in pentane); IR (neat) 2964, 2926, 2856, 1714 (C=O), 1463, 1382, 1015, 722. Anal. calcd for C₁₆H₃₂O C, 79.93; H, 13.42. found C, 79.77; H, 13.35.

2,4-Dimethyl-3-tetradodecanone: ¹H NMR δ 0.88 (t, *J* = 7.2 Hz, 3H, CH₂CH₃), 1.00–1.11 (m, 9H, CH(CH₃)₂, CHCH₃), 1.32–1.43 (m, 18H, (CH₂)₉), 2.63–2.77 (m, 2H, CHC(=O)CH); ¹³C NMR δ 14.1, 16.8, 18.2, 18.4, 22.7, 27.5, 29.4, 29.5, 29.6 (2C), 29.7, 31.9, 33.2, 39.6, 44.6, 218.7.

(3) Morisson, V.; Barnier, J. P.; Blanco, L. *Tetrahedron*, **1998**, *54*, 7749–7764.

The reaction was carried out according to procedure B on a 1.0-mmol scale by using the corresponding imine (0.198 g, 1.0 mmol) and 1-chlorodecane (0.212 g, 1.2 mmol). Conditions; 50 °C, 24 h, 65 °C, 12 h. The title compound (0.226 g, 94% yield, 85:15 mixture determined by ^1H NMR analysis) was obtained as a colorless liquid after silica gel column chromatography.

2-Decyl-5-methylcyclohexanone (13)

The reaction was carried out according to procedure B on a 1.0-mmol scale by using the corresponding imine (0.210 g, 1.0 mmol) and 1-fluorodecane (0.192 g, 1.2 mmol). Conditions; 65 °C, 36 h. The title compound (0.235 g, 93% yield, *cis:trans* = 72:28 determined by ^1H NMR analysis) was obtained as a colorless liquid after silica gel column chromatography. R_f = 0.47 (*cis* isomer), 0.65 (*trans* isomer) (10% Et₂O in pentane); IR (neat) 2922, 2853, 1714 (C=O), 1455, 1378, 1127, 984, 857, 722; Anal. calcd for C₁₇H₃₂O C, 80.88; H, 12.78. found C, 80.76; H, 12.96.

cis isomer: ^1H NMR δ 0.88 (t, J = 6.9 Hz, 3H, CH₂CH₃), 1.00 (d, J = 6.3 Hz, 3H, CHCH₃), 1.08–1.18 (m, 1H, CHCHH(CH₂)₈), 1.18–1.40 (m, 18H, CHCHHCH₂CHHCH (axial), (CH₂)₈CH₃), 1.65–1.86 (m, 3H, CHCH₂CH₂CH₂CH, CHH(CH₂)₈CH₃), 2.18–2.18 (m, 2H, CHCHHCH₂CHHCH (equatorial)), 2.19–2.28 (m, 1H, CH(CH₂)₉), 2.34–2.44 (m, 1H, CHCH₃); ^{13}C NMR δ 14.1, 14.5, 22.7, 25.6, 27.3, 29.1, 29.3, 29.5, 29.6 (2C), 29.9, 31.9, 35.2, 37.5, 45.6, 50.8, 214.4.

trans isomer: ^1H NMR δ 0.88 (t, J = 6.9 Hz, 3H, CH₂CH₃), 1.05 (d, J = 6.3 Hz, 3H, CHCH₃), 1.10–1.20 (m, 1H, CHH(CH₂)₈CH₃), 1.18–1.33 (m, 16H, (CH₂)₈CH₃), 1.33–1.48 (m, 2H, CHCHHCH₂CHHCH (axial)), 1.64–1.88 (m, 4H, CH₃CHCH₂CH₂CHHCH, CHH(CH₂)₈CH₃), 1.94–2.02 (m, 1H, CH(CH₃)CHH (equatorial)), 2.37–2.44 (m, 1H, CH(CH₂)₉), 2.49–2.57 (m, 1H, CHCH₃); ^{13}C NMR δ 14.1, 15.3, 20.5, 22.7, 27.3, 29.3, 29.5, 29.6 (3C), 30.9, 31.9, 32.4, 35.6, 42.2, 49.5, 217.0.

The reaction was carried out according to procedure B on a 1.0-mmol scale by using the corresponding imine (0.210 g, 1.0 mmol) and 1-chlorodecane (0.212 g, 1.2 mmol). Conditions; 50 °C, 24 h, 65 °C, 12 h. The title compound (0.232 g, 92% yield, *cis/trans* = 50: 50 determined by ^1H NMR analysis) was obtained as a colorless liquid after silica gel column chromatography.

4,5-Dimethyldodecan-3-one (14)⁴

The reaction was carried out according to procedure B on a 1.0-mmol scale by using imine (0.184 g, 1.0 mmol) and 2-chloroheptane (0.162 g, 1.2 mmol). Conditions; 45 °C, 24 h, 60 °C, 12 h. The title compound (0.131 g, 71% yield, *syn:anti* = 58:42 determined by ¹H NMR analysis) was obtained as a colorless liquid after silica gel column chromatography.

3-Ethyl-2-phenylheptan-4-one (15)⁵

The reaction was carried out according to procedure B on a 1.0-mmol scale by using the corresponding imine (0.212 g, 1.0 mmol) and (1-chloroethyl)benzene (0.211 g, 1.5 mmol). Conditions; 30 °C, 12 h, 50 °C, 3 h. The title compound (0.186 g, 85% yield, *syn:anti* = 70:30 determined by ¹H NMR analysis) was obtained as a colorless liquid after silica gel column chromatography. *R*_f = 0.50 (10% Et₂O in pentane); IR (neat) 3065 and 3030 (aromatic C–H), 2964, 2934, 2876, 1710 (C=O), 1494, 1455, 1378, 1270, 1127, 1027, 760, 698.

syn isomer: ¹H NMR δ 0.64 (t, *J* = 7.5 Hz, 3H, CH₂CH₂CH₃), 0.81 (t, *J* = 7.5 Hz, 3H, CHCH₂CH₃), 1.25 (d, *J* = 6.9 Hz, 3H, CHCH₃), 1.18–1.33 (m, 2H, CH₂CH₂CH₃), 1.58–1.73 (m, 2H, CHCH₂CH₃), 1.79–1.88 (m, 1H, CCHHCH₂), 2.03–2.12 (m, 1H, CCHHCH₂), 2.58–2.67 (m, 1H, CCHCH₂), 2.87–2.97 (m, 1H, CHPh), 7.13–7.18 (m, 3H, CHCHCHCHCH), 7.23–7.27 (m, 2H, CHCHCHCHCH); ¹³C NMR δ 11.9, 13.5, 16.2, 18.8, 22.5, 41.7, 46.6, 60.8, 126.2, 127.4 (2C), 128.3 (2C), 145.4, 214.5.

anti isomer: ¹H NMR δ 0.70 (t, *J* = 7.5 Hz, 3H, CH₂CH₂CH₃), 0.93 (t, *J* = 7.5 Hz, 3H, CHCH₂CH₃), 1.16 (d, *J* = 6.9 Hz, 3H, CHCH₃), 1.25–1.45 (m, 2H, CH₂CH₂CH₃), 1.57–1.66 (m, 2H, CHCH₂CH₃), 2.37–2.43 (m, 2H, CCH₂CH₂), 2.58–2.67 (m, 1H, CCHCH₂), 2.87–2.97 (m, 1H, CHPh), 7.17–7.31 (m, 5H, (CH)₅); ¹³C NMR δ 11.6, 13.8, 16.5, 20.4, 24.2, 42.1, 46.5, 60.3, 126.3, 127.4 (2C), 128.4 (2C), 145.1, 214.9.

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8-*tert*-Butyldimethylsilyloxy-4-methyloctan-3-one (16)⁶

The reaction was carried out according to procedure B on a 1.0-mmol scale by using the corresponding imine (0.184 g, 1.0 mmol) and *tert*-butyl-(4-chlorobutoxy)dimethylsilane (0.267 g, 1.2 mmol). Conditions; 50 °C, 24 h, 65 °C, 12 h. The title compound (0.253 g, 93% yield) was obtained as a colorless liquid after silica gel column chromatography.

6-*tert*-Butyldimethylsilyloxy-4-methylhexan-3-one (17)

The reaction was carried out according to procedure B on a 1.0-mmol scale by using the corresponding imine (0.184 g, 1.0 mmol) and *tert*-butyl-(2-chloroethoxy)dimethylsilane (0.238 g, 1.2 mmol). Conditions; 50 °C, 24 h, 65 °C, 12 h. The title compound (0.131 g, 68% yield) was obtained as a colorless liquid after silica gel column chromatography. R_f = 0.35 (10% Et₂O in pentane); IR (neat) 2957, 2934, 2860, 1714 (C=O), 1463, 1254, 1096, 899, 834, 776; ¹H NMR δ 0.03 (s, 6H, Si(CH₃)₂), 0.88 (s, 9H, C(CH₃)₃), 1.04 (t, J = 7.2 Hz, 3H, CH₂CH₃), 1.08 (d, J = 7.4 Hz, 3H, CHCH₃), 1.46–1.54 (m, 1H, CHCHH), 1.87–1.94 (m, 1H, CHCHH), 2.45–2.53 (m, 2H, CCH₂), 2.69–2.78 (m, 1H, CCH), 3.59 (t, J = 7.2 Hz, 2H, CH₂OSi); ¹³C NMR δ –5.5 (2C), 7.8, 16.5, 18.2, 25.9 (3C), 34.3, 35.8, 42.4, 60.7, 215.1. Anal. calcd for C₁₃H₂₈O₂Si C, 63.87; H, 11.55. found C, 64.04; H, 11.35.

4-Dimethylamino-2-methyl-1-phenylbutan-1-one (18)

N-(1-Phenylpropylidene)-*N,N*-diethyl-1,2-ethanediamine (0.629 g, 3.08 mmol) was added to *tert*-BuMgCl (2.12 M in THF, 1.44 mL, 3.08 mmol) at –78 °C. The mixture was stirred at 0 °C for 1 h,

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and then warmed to room temperature. The reaction mixture was transferred to the alkyl chloride, prepared from *tert*-BuMgCl (2.12 M in THF, 1.04 mL, 2.2 mmol) and *N*-(2-Chloroethyl)dimethylamine hydrochloride (0.317 g, 2.2 mmol) in THF (1.0 mL), via cannula at room temperature and rinsed with THF (0.5 mL) twice. The reaction mixture was heated at 50 °C for 36 h. AcOH in H₂O (50 wt%, 2.0 mL) was added slowly at 0 °C. The reaction mixture was stirred at 50 °C for 1 h then cooled to room temperature. H₂O (8.0 mL) was added and the aqueous layer was washed with pentane three times to remove propiophenone. To the aqueous layer was added 3N NaOH until pH >12. The aqueous layer was extracted with Et₂O five times. The combined extracts were filtered with a pad of Na₂SO₄ by using Et₂O as an eluent. Gas chromatography analysis was carried out (77% yield) by using undecane as an internal standard. The solvent was removed *in vacuo*. The title compound (0.310 g, 69 % yield) was obtained as a colorless liquid after Kurgelour distillation.; Bp 140 °C/5 mmHg; R_f = 0.17 (100% MeOH); IR (neat) 3065 (aromatic C–H), 2968, 2941, 2860, 2818, 2768, 1679 (C=O), 1598, 1579, 1447, 1370, 1220, 1177, 1042, 973, 795, 703; ¹H NMR δ 1.21 (d, *J* = 6.9 Hz, 3H, CHCH₃), 1.54–1.61 (m, 1H, CHCHH), 1.99–2.06 (m, 1H, CHCHH), 2.17 (s, 6H, N(CH₃)₂), 2.22–2.39 (m, 2H, NCH₂), 3.57 (sext, *J* = 6.9 Hz, 1H, CHCH₃), 7.46 (brt, *J* = 7.5 Hz, 2H, CH(CH)₃CH), 7.55 (brt, *J* = 7.5 Hz, 1H, (CH)₂CH(CH)₂), 7.97 (brd, *J* = 7.5 Hz, 2H, CHCHCHCHCH); ¹³C NMR δ 17.5, 31.6, 38.6, 45.4 (2C), 57.4, 128.2 (2C), 128.5 (2C), 132.7, 136.8, 204.2. Anal. calcd for C₁₃H₁₉NO C, 76.06; H, 9.33; N 6.82, found C, 75.99; H, 9.39; N, 6.77.

(3*S*)-1,3-Diphenylbutan-1-one (20)⁷

The starting alkyl halide, (1*S*)-(1-chloroethyl)benzene, was prepared according to the literature procedure⁸ from (1*R*)-1-phenylethanol in 46% yield. The enantiomeric excess of the chloride was determined as 94.0% ee by GC analysis (γ-DEX 225, Supelco, 30 m × 0.25 mm i.d., 0.25 μm film; detector, FID at 220 °C; column temperature, 70 °C for 60 min). Peaks at the retention times of 31.1 and 32.4 min, which correspond to the enantiomers, were observed in a 97.0:3.0 ratio.

N'-(1-Phenylethylidene)-*N,N*-diethyl-1,2-ethanediamine (0.131 g, 0.6 mmol) was added to *tert*-BuMgCl (2.06 M in THF, 0.29 mL, 0.6 mmol) at –78 °C. The mixture was stirred at 0 °C for 1 h, and

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then warmed to room temperature. After 1 h, (1*S*)-(1-chloroethyl)benzene (0.070 g, 0.5 mmol, 94.0% *ee*) was added at room temperature. The reaction mixture was stirred at 30 °C for 24 h, 40 °C, 6 h, and 50 °C, 6 h. AcOH in H₂O (50 wt%, 0.5 mL) was added slowly at 0 °C. The reaction mixture was stirred at 50 °C for 1 h then cooled to room temperature. The reaction mixture was neutralized with saturated NaHCO₃ aqueous solution. The aqueous layer was extracted with Et₂O five times. The combined organic extracts were dried with Na₂SO₄. After the solvents were removed *in vacuo*, the crude product was chromatographed on silica gel (5 g, pentane and then 3% Et₂O in pentane) to obtain the title compound (0.073 g, 65% yield, 88.5% *ee*) as a colorless liquid. The enantiomeric excess of the compound was determined as 88.5% *ee* by HPLC analysis (CHRALCEL OJ-H, Daicel, 4.6 × 250 mm; column temperature, 15 °C; eluent, hexane:*i*-PrOH = 99:1; flow rate, 0.3 mL/min; detector, 254 nm (UV)). Peaks at the retention times of 49.3 and 63.8 min, which correspond to the enantiomers, were observed in a 94.25:5.75 ratio.; $[\alpha]_D^{26} +12.43$ (C = 0.58, CCl₄). The starting alkyl chloride was recovered (30% ¹H NMR yield, 80.6% *ee*).