Asymmetric Aza-Michael Reactions Catalysed by Cinchona Alkaloids

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General methods. NMR spectra were acquired running at 400 and 100 MHz for ^1H and ^{13}C , respectively. Chemical shifts (δ) are reported in ppm relative to CDCl_3 ($\delta = 7.26$) for ^1H NMR and relative to the central resonance of CDCl_3 ($\delta = 77.0$) for ^{13}C NMR. ^{13}C NMR spectra were acquired on a broad band decoupled mode. Mass spectra were recorded using electrospray (ES^+) ionization techniques. Analytical thin layer chromatography (TLC) was performed using pre-coated aluminium-backed plates and visualized by ultraviolet irradiation or I_2 vapours exposure unless otherwise stated. Optical rotations were measured on a polarimeter. The enantiomeric excess (ee) of the products was determined by chiral stationary phase HPLC (Daicel Chiralpak AD or Daicel Chiralcel OD and OJ columns) or a GC Chrompak CP-Chirasil Dex CB-column.

Materials. Analytical grade solvents were used as received. For flash chromatography (FC) silica gel 60, 230-400 mesh was used. Catalysts **I**,¹ **II**² and **VI**³ were prepared as reported in literature; catalysts **III**, **IV**, **V**, **VII**, **VIII** are commercially available and were used as received. Hydrazones **1a-e** were prepared from the corresponding aldehydes and methyl hydrazine according to literature methods.⁴ Enones **2a-c,g** were used as received; enones **2d**,⁵ **2f**,⁶ **2e**⁷ (from 6,6-dimethylcyclohexane-1,3-dione), **2h**⁸ were synthesized according to literature methods.

1-(3,4-Dichlorobenzylidene)-2-methylhydrazine **1e**.

Yellow oil. ^1H NMR (CDCl_3) δ 7.63 (d, 2 Hz, 1H), 7.4-7.3 (m, 3H), 5.54 (1H, broad s, 1H), 2.97 (s, 3H). ^{13}C NMR (CDCl_3) δ 136.9, 132.8, 131.3, 130.9, 130.6, 127.2, 125.0. HRMS: $\text{C}_8\text{H}_8\text{Cl}_2\text{N}_2$ $[\text{M}+\text{H}]^+$ calcd.: 203.0143, found: 203.0154.

3-(2-Benzylidene-1-methylhydrazinyl)cyclopentanone **3ab**.

The title compound was obtained according to the general procedure (hydrazone 0.25 M, reaction for 3 d); the crude product was purified by FC on silica eluting with Et₂O:pentane 1:1 to give **3ab** as a colourless oil, yield 87%. ¹H NMR (C₆D₆) δ 7.31 (d, J 7.2 Hz, 2H), 6.90 (t, J 7.2 Hz, 2H), 6.75 (t, J 7.2 Hz, 1H), 6.67 (s, 1H), 2.90-2.80 (m, 1H), 2.22 (dd, J_{vic} 5.2 Hz, J_{gem} 18 Hz, 1H), 1.89 (s, 3H), 1.90-1.80 (m, 1H), 1.70 (dd, J_{vic} 7.2 Hz, J_{gem} 18 Hz, 1H), 1.50-1.35 (m, 2H), 1.25-1.0 (1H, m). ¹³C NMR (CDCl₃) δ 218.1, 137.0, 133.6, 128.8, 127.7, 125.9, 64.4, 43.9, 37.5, 36.5, 26.7. HRMS: C₁₃H₁₆N₂O [M+H]⁺ calcd.: 217.1341, found: 217.1343; [M+Na]⁺ calcd.: 239.1160, found: 239.1155. [α]_D²⁰ -50.3 (c = 1.0, CHCl₃, 31% ee). The ee was determined by HPLC using a Chiralcel OD column [hexane:iPrOH (90:10)]; flow rate 1.0 mL/min; τ_{minor} = 9.9 min, τ_{major} = 10.8 min (31% ee).

3-(1-Methyl-2-(4-nitrobenzylidene)hydrazinyl)cyclohexanone **3ba**.

The title compound was obtained according to the general procedure (hydrazone 1 M, reaction for 5 d); the crude product was purified by FC on silica eluting with Et₂O:pentane 1:1 to give **3ba** as an orange solid, yield 75%. ¹H NMR (CDCl₃) δ 8.12 (d, J 9 Hz, 2H), 7.54 (d, J 9 Hz, 2H), 7.11 (s, 1H), 3.85-3.65 (m, 1H), 2.98 (s, 3H), 2.78 (dd, J_{vic} 8 Hz, J_{gem} 14.4 Hz, 1H), 2.59 (dd, J_{vic} 4.8 Hz, J_{gem} 14.4 Hz, 1H), 2.45-2.25 (m, 2H), 2.05-1.85 (m, 3H), 1.70-1.50 (m, 1H). ¹³C NMR (CDCl₃) δ 209.4, 145.7, 144.2, 126.6, 125.4, 124.1, 65.3, 46.1, 40.8, 36.4, 28.7, 21.3. HRMS: C₁₄H₁₇N₃O₃ [M+Na]⁺ calcd.: 298.1168, found: 298.1166. [α]_D²⁰ -104.1 (c = 1.0, CHCl₃, 74% ee). The ee was determined by HPLC using a Chiralcel OD column [hexane:iPrOH (90:10)]; flow rate 1.0 mL/min; τ_{minor} = 26.6 min, τ_{major} = 27.9 min (74% ee).

3-(1-Methyl-2-(4-chlorobenzylidene)hydrazinyl)cyclohexanone **3ca**.

The title compound was obtained according to the general procedure (hydrazone 0.5 M, reaction for 3 d); the crude product was purified by FC on silica eluting with Et₂O:pentane 1:1 to give **3ca** as a white solid, yield 89%. ¹H NMR (CDCl₃) δ 7.43 (d, J 8.8 Hz, 2H), 7.27 (d, J 8.8 Hz, 2H), 7.15 (s, 1H), 3.65-3.50 (m, 1H), 2.91 (s, 3H),

2.77 (dd, J_{vic} 9.2 Hz, J_{gem} 14.4 Hz, 1H), 2.58 (dd, J_{vic} 4.8 Hz, J_{gem} 14.4 Hz, 1H), 2.45-2.25 (m, 2H), 2.05-1.85 (m, 3H), 1.70-1.50 (m, 1H). ¹³C NMR (CDCl₃) δ 210.0, 136.1, 132.5, 129.8, 128.8, 126.9, 65.3, 46.2, 41.0, 36.5, 28.6, 21.7. HRMS: C₁₄H₁₇ClN₂O [M+Na]⁺ calcd.: 287.0927, found: 287.0916. [α]_D²⁰ -98.8 (c = 1.0, CHCl₃, 84% ee). The ee was determined by HPLC using a Chiralpak AD column [hexane:*i*PrOH (98:2)]; flow rate 1.0 mL/min; τ_{minor} = 20.4 min, τ_{major} = 22.7 min (84% ee after crystallization from Et₂O).

3-(1-Methyl-2-(4-bromobenzylidene)hydrazinyl)cyclohexanone **3da**.

The title compound was obtained according to the general procedure (hydrazone 0.5 M, reaction for 3 d); the crude product was purified by FC on silica eluting with Et₂O:pentane 1:1 to give **3da** as a white solid, yield 82%. ¹H NMR (CDCl₃) δ 7.40-7.25 (m, 4H), 7.05 (s, 1H), 3.60-3.50 (m, 1H), 2.83 (s, 3H), 2.71 (dd, J_{vic} 8.8 Hz, J_{gem}

14.4 Hz, 1H), 2.51 (dd, J_{vic} 4.8 Hz, J_{gem} 14.4 Hz, 1H), 2.40-2.20 (m, 2H), 2.00-1.80 (m, 3H), 1.70-1.50 (m, 1H). ¹³C NMR (CDCl₃) δ 210.1, 136.5, 131.7, 129.9, 127.2, 120.7, 65.3, 46.2, 41.0, 36.6, 28.6, 21.7. HRMS: C₁₄H₁₇BrN₂O [M+Na]⁺ calcd.: 331.0422, found: 331.0417. [α]_D²⁰ -88.4 (c = 1.0, CHCl₃, 81% ee). The ee was determined by HPLC using a Chiralpak AD column [hexane:*i*PrOH (98:2)]; flow rate 1.0 mL/min; τ_{minor} = 21.4 min, τ_{major} = 23.8 min (81% ee after crystallization from Et₂O).

3-(1-Methyl-2-(3,4-dichlorobenzylidene)hydrazinyl)cyclohexanone **3ea**.

The title compound was obtained according to the general procedure (hydrazone 0.5 M, reaction for 3 d); the crude product was purified by FC on silica eluting with Et₂O:pentane 1:1 to give **3ea** as a white solid, yield 86%. ¹H NMR (CDCl₃) δ 7.5–7.2 (m, 3H), 7.02 (s, 1H), 3.65–3.50 (m, 1H), 2.86 (s, 3H), 2.71 (dd, J_{vic} 9.6 Hz, J_{gem}

14.4 Hz, 1H), 2.53 (dd, J_{vic} 4.8 Hz, J_{gem} 14.4 Hz, 1H), 2.45–2.25 (m, 2H), 2.05–1.85 (m, 3H), 1.65–1.50 (m, 1H). ¹³C NMR (CDCl₃) δ 209.8, 137.8, 132.5, 130.5, 130.0, 127.8, 126.9, 124.8, 65.3, 46.2, 40.9, 36.4, 28.7, 21.6. HRMS: C₁₄H₁₆Cl₂N₂O [M+Na]⁺ calcd.: 321.0537, found: 312.0538. [α]_D²⁰ –61.3 (c = 1.0, CHCl₃, 68% ee). The ee was determined by HPLC using a Chiralpak AD column [hexane:*i*PrOH (98:2)]; flow rate 1.0 mL/min; τ_{minor} = 21.8 min, τ_{major} = 23.6 min (68% ee).

5-(2-Benzylidene-1-methylhydrazinyl)-3,3-dimethylcyclohexanone **3ad**.

The title compound was obtained according to the general procedure (hydrazone 0.5 M, reaction for 3 d); the crude product was purified by FC on silica eluting with Et₂O:pentane 2:8 to give **3ad** as a white solid, yield 83%. ¹H NMR (CDCl₃) δ 7.6–7.54 (m, 2H), 7.38–7.30

(m, 3H), 7.26–7.20 (m, 1H), 3.7–3.55 (m, 1H), 2.91 (s, 3H), 2.8–2.7 (m, 1H), 2.6–2.5 (m, 1H), 2.35–2.25 (m, 1H), 2.2–2.1 (m, 1H), 2.05–1.90 (m, 1H), 1.85–1.75 (m, 1H), 1.13, 0.93 (s, 3H). ¹³C NMR (CDCl₃) δ 210.9, 137.3, 132.8, 128.7, 127.6, 125.8, 63.0, 54.5, 45.2, 42.2, 37.2, 33.1, 32.3, 26.1. HRMS: C₁₆H₂₂N₂O [M+Na]⁺ calcd.: 281.1630, found: 281.1635. [α]_D²⁰ –15.9 (c = 1.0, CHCl₃, 76% ee). The ee was determined by HPLC using a Chiralcel OJ column [hexane:*i*PrOH (98:2)]; flow rate 1.0 mL/min; τ_{minor} = 21.1 min, τ_{major} = 23.9 min (76% ee).

5-(2-Benzylidene-1-methylhydrazinyl)-2,2-dimethylcyclohexanone **3ae**.

The title compound was obtained according to the general procedure (hydrazone 0.5 M, reaction for 4 d); the crude product was purified by FC on silica eluting with Et₂O:pentane:\CH₂Cl₂ 1:7:2 to give **3ae** as a white solid, yield 77%. ¹H NMR (CDCl₃)

δ 7.60-7.50 (m, 2H), 7.35-7.25 (m, 2H), 7.25-7.15 (m, 2H), 3.60-3.40 (m, 1H), 2.93 (dd, J 9.4 Hz, J 14.4 Hz, 1H), 2.85 (s, 3H), 2.53 (ddd, J 1.2 Hz, J 4.8 Hz, J 14.4 Hz, 1H), 2.20-2.00 (m, 1H), 1.95-1.80 (m, 1H), 1.75-1.65 (m, 1H), 1.50-1.35 (m, 1H), 1.16, 1.08 (s, 3H). ¹³C NMR δ 214.3, 137.4, 131.7, 128.7, 127.4, 125.8, 66.0, 44.6, 42.6, 36.7, 36.3, 25.5, 25.3, 25.2. HRMS: C₁₆H₂₂N₂O [M+Na]⁺ calcd.: 281.1630, found: 281.1631. [α]_D²⁰ -37.9 (c = 1.0, CHCl₃, 60% ee). The ee was determined by HPLC using a Chiralcel OJ column [hexane/*i*PrOH (98:2)]; flow rate 1.0 mL/min; τ_{major} = 19.1 min, τ_{minor} = 23.4 min (60% ee).

3-(2-Benzylidene-1-methylhydrazinyl)-5-isopropylcyclohexanone *cis*-**3af** and *trans*-**3af**.

The title compound was obtained according to the general procedure (hydrazone 0.5 M, reaction for 3 d); the crude product (mixture of diastereoisomers *trans* : *cis* = 62:38 as determined by NMR) was purified by FC on silica (eluent: gradual polarity change

from pentane to Et₂O) to give *trans*-**3af** (yield 63%) and *cis*-**3af** (yield 36%) as colourless oils. Enone **2f** in excess was recovered quantitatively; [α]_D²⁰ +2.5 (c = 1.0, CHCl₃, 7% ee). GC Chrompak CP-Chirasil Dex CB-column. Temperature program: from 70 C° to 140 C° at a rate of 10 C°/min maintained temperature for 10 min. then to 180 C° at a rate of 10 C°/min. τ_{major} = 7.9 min, τ_{minor} = 8.0 min (7% ee).

***cis*-3-(2-Benzylidene-1-methylhydrazinyl)-5-isopropylcyclohexanone 3af.**

^1H NMR (CDCl_3) δ 7.60-7.54 (m, 2H), 7.36-7.28 (m, 3H), 7.26-7.20 (m, 1H), 3.5-3.4 (m, 1H), 2.91 (s, 3H), 2.8-2.7 (m, 1H), 2.65-2.55 (m, 1H), 2.45-2.35 (m, 1H), 2.15-2.05 (m, 1H), 1.8-1.45 (m, 4H), 0.94, 0.92 (d, J 3.6 Hz, 3H). ^{13}C NMR (CDCl_3) δ

211.2, 137.2, 132.7, 128.7, 127.6, 125.8, 65.5, 45.8, 44.9, 40.8, 36.8, 33.0, 32.7, 19.8, 19.6. HRMS: $\text{C}_{17}\text{H}_{24}\text{N}_2\text{O}$ $[\text{M}+\text{Na}]^+$ calcd.: 295.1786, found: 295.1797. $[\alpha]_{\text{D}}^{20} +9.4$ ($c = 1.0$, CHCl_3 , 76% ee). The ee was determined by HPLC using a Chiralcel OD column [hexane:*i*PrOH (98:2)]; flow rate 1.0 mL/min; $\tau_{\text{minor}} = 10.3$ min, $\tau_{\text{major}} = 11.7$ min (76% ee).

***trans*-3-(2-Benzylidene-1-methylhydrazinyl)-5-isopropylcyclohexanone 3af.**

^1H NMR (CDCl_3) δ 7.48-7.42 (m, 2H), 7.36-7.28 (m, 2H), 7.22-7.12 (m, 1H), 3.95-3.85 (m, 1H), 2.92 (s, 3H), 2.85-2.75 (m, 1H), 2.55-2.45 (m, 2H), 2.20-2.10 (m, 1H), 2.10-2.00 (m, 1H), 1.85-1.75 (m, 1H), 1.65-1.35 (m, 2H), 0.87, 0.85 (d, J 4.8 Hz, 3H). ^{13}C

NMR δ 210.3, 137.6, 130.9, 128.8, 127.2, 125.9, 62.7, 45.4, 44.8, 38.1, 36.7, 32.0, 31.0, 19.9, 19.7. HRMS: $\text{C}_{17}\text{H}_{24}\text{N}_2\text{O}$ $[\text{M}+\text{Na}]^+$ calcd.: 295.1786, found: 295.1770. $[\alpha]_{\text{D}}^{20} -23.6$ ($c = 1.0$, CHCl_3 , 62% ee). The ee was determined by HPLC using a Chiralcel OJ column [hexane:*i*PrOH (99:1)]; flow rate 1.0 mL/min; $\tau_{\text{major}} = 20.8$ min, $\tau_{\text{minor}} = 24.6$ min (62% ee).

3-(2-Benzylidene-1-methylhydrazinyl)cycloheptanone 3ag.

The title compound was obtained according to the general procedure (hydrazone 0.5 M, reaction for 3 d); the crude product was purified by FC on silica eluting with Et_2O :pentane 4:6 to give **3ag** as a colourless oil,

yield 81%. ^1H NMR (CDCl_3) δ 7.52-7.44 (m, 2H), 7.28-7.22 (m, 2H), 7.16 (s, 1H), 7.20-7.10 (m, 1H), 3.50-3.40 (m, 1H), 2.92 (dd, J_{vic} 10.4 Hz, J_{gem} 14 Hz, 1H), 2.77 (s, 3H), 2.64-2.54 (m, 1H), 2.55-2.45 (m, 1H), 2.41 (dd, J_{vic} 4.0 Hz, J_{gem} 14 Hz, 1H), 2.06-1.78 (m, 4H), 1.70-1.56 (m, 1H), 1.46-1.34 (m, 1H). ^{13}C NMR δ 213.2, 137.3, 132.3, 128.7, 127.5, 125.8, 64.3, 48.2, 44.3, 35.9, 35.1, 27.0, 24.4. HRMS: $\text{C}_{15}\text{H}_{20}\text{N}_2\text{O}$ $[\text{M}+\text{H}]^+$ calcd.: 245.1654, found: 245.1650; $[\text{M}+\text{Na}]^+$ calcd.: 267.1473, found: 267.1476. $[\alpha]_{\text{D}}^{20}$ -19.2 ($c = 1.0$, CHCl_3 , 72% ee). The ee was determined by HPLC using a Chiralcel OJ column [hexane:*i*PrOH (98:2)]; flow rate 1.0 mL/min; $\tau_{\text{minor}} = 42.4$ min, $\tau_{\text{major}} = 47.9$ min (72% ee).

3-(2-Benzylidene-1-methylhydrazinyl)cyclooctanone **3ah**.

The title compound was obtained according to the general procedure (hydrazone 0.5 M, reaction for 3 d); the crude product was purified by FC on silica eluting with Et_2O :pentane: CH_2Cl_2 1:6:3 to give **3ah** as a colourless oil, yield 83%. ^1H NMR (CDCl_3) δ 7.55-7.45 (m, 2H),

7.30-7.20 (m, 2H), 7.20-7.15 (m, 2H), 3.60-3.45 (m, 1H), 3.02 (t, J 11.6 Hz, 1H), 2.82 (s, 3H), 2.50-2.25 (m, 3H), 2.20-2.00 (m, 1H), 1.97-1.70 (m, 3H), 1.67-1.35 (m, 3H), 1.25-1.05 (m, 1H). ^{13}C NMR δ 215.1, 137.4, 132.1, 128.7, 127.4, 125.8, 67.2, 44.5, 44.1, 36.4, 30.9, 28.2, 23.5, 22.2. HRMS: $\text{C}_{16}\text{H}_{22}\text{N}_2\text{O}$ $[\text{M}+\text{Na}]^+$ calcd.: 281.1630, found: 281.1641. $[\alpha]_{\text{D}}^{20}$ +1.9 ($c = 1.0$, CHCl_3 , 77% ee). The ee was determined by HPLC using two Chiralcel OD columns [hexane:*i*PrOH (99:1)]; flow rate 0.75 mL/min; $\tau_{\text{minor}} = 29.8$ min, $\tau_{\text{major}} = 32.6$ min (77% ee).

3-(1-Methyl-2-(4-nitrobenzylidene)hydrazinyl)cyclohexanol **4ba**.

The title compound was obtained according to the general procedure; the crude product (mixture of diastereoisomers *trans*:*cis* = 7:93 as determined by NMR) was purified by FC on silica (eluent: Et_2O / CH_2Cl_2 8\2) to give *trans*-**4ba** (yield 7%) and *cis*-**4ba** (yield 93%) as yellow oils.

***trans*-3-(1-Methyl-2-(4-nitrobenzylidene)hydrazinyl)cyclohexanol.**

^1H NMR (CDCl_3) δ 8.07 (d, J 8.8 Hz, 2H), 7.53 (d, J 8.8 Hz, 2H), 7.03 (s, 1H), 4.35-4.20 (m, 1H), 3.70-3.60 (m, 1H), 2.91 (s, 3H), 2.00-1.30 (m, 9H). ^{13}C NMR (CDCl_3) δ 145.7, 144.6, 125.7, 125.1, 124.3, 67.5, 61.8, 37.5, 36.1, 32.5, 30.8, 19.7. HRMS: $\text{C}_{14}\text{H}_{19}\text{N}_3\text{O}_3$

$[\text{M}+\text{Na}]^+$ calcd.: 300.1324, found: 300.1329. $[\alpha]_{\text{D}^{20}} -7.5$ ($c = 1.0$, CHCl_3 , 72% ee). The ee was determined by HPLC using a Chiralcel OD column [hexane:*i*PrOH (95:5)]; flow rate 1.0 mL/min; $\tau_{\text{major}} = 23.9$ min, $\tau_{\text{minor}} = 28.8$ min (72% ee).

***cis*-3-(1-Methyl-2-(4-nitrobenzylidene)hydrazinyl)cyclohexanol.**

^1H NMR (CDCl_3) δ 8.08 (d, J 8.8 Hz, 2H), 7.55 (d, J 8.8 Hz, 2H), 7.08 (s, 1H), 3.70-3.55 (m, 1H), 3.40-3.25 (m, 1H), 2.89 (s, 3H), 2.25-1.10 (m, 9H). ^{13}C NMR (CDCl_3) δ 145.8, 144.4, 126.2, 125.3, 124.3, 70.0, 65.3, 40.1, 35.4, 35.1, 29.8, 22.0. HRMS:

$\text{C}_{14}\text{H}_{19}\text{N}_3\text{O}_3$ $[\text{M}+\text{Na}]^+$ calcd.: 300.1324, found: 300.1319. $[\alpha]_{\text{D}^{20}} -45.0$ ($c = 1.0$, CHCl_3 , 72% ee). The ee was determined by HPLC using a Chiralcel OD column [hexane:*i*PrOH (90:10)]; flow rate 1.0 mL/min; $\tau_{\text{minor}} = 15.5$ min, $\tau_{\text{major}} = 27.3$ min (72% ee).

3-(1-Methyl-2-(4-nitrobenzylidene)hydrazinyl)cyclohexyl 4-bromobenzoate 5ba.

cis-**4ba** (0.35 mmol) was dissolved with 5 mL of CH_2Cl_2 and 1 mL of Et_3N in a glass vial equipped with a magnetic stirring bar; at the resulting solution was added 4-bromo-benzoylchloride (1.3 equiv). After 1 h

the reaction was completed; the solvent was removed at low pressure and the crude product was washed with water and extracted with CH_2Cl_2 (2 x 25 mL). The combined organic layers were dried

(MgSO₄) and evaporated. The pure product **5ba** was obtained by flash chromatography on SiO₂ (eluent: CH₂Cl₂/pentane 1/1) as yellow solid; yield: 96%, ee: 72%. After crystallization with Et₂O the ee increased to 97%.

¹H NMR (CDCl₃) δ 8.14 (d, J 8.8 Hz, 2H), 7.88 (d, J 8.8 Hz, 2H), 7.61 (d, J 8.8 Hz, 2H), 7.56 (d, J 8.8 Hz, 2H), 7.13 (s, 1H), 5.05-4.95 (m, 1H), 3.50-3.35 (m, 1H), 2.97 (s, 1H), 2.40-1.35 (m, 9H).

¹³C NMR (CDCl₃) δ 165.4, 145.9, 144.3, 131.9, 131.3, 129.6, 128.2, 126.6, 125.3, 124.3, 73.1, 65.1, 36.5, 35.9, 31.4, 29.9, 22.0. HRMS: C₂₁H₂₂BrN₃O₄ [M+Na]⁺ calcd.: 482.0691, found: 482.0689. [α]_D²⁰ -153.3 (c = 1.0, CHCl₃, 97% ee). The ee was determined by HPLC using a Chiralcel AD column [hexane:*i*PrOH (95:5)]; flow rate 1.0 mL/min; τ_{minor} = 27.7 min, τ_{major} = 33.9 min (97% ee after crystallization from Et₂O).

X-Ray Structure of 3ca.

Hydrazone 1b in CDCl₃

Hydrazone 1b + catalyst VII (1:1) in CDCl₃

Hydrazone 1b + catalyst VII (1:1) in CDCl₃

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