Supporting Information
for DOI: 10.1055/s-0030-1258084
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Supporting Information for

SmI₂-Mediated Reductive Cross-Coupling Reactions of α-Cyclopropyl Nitrones

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General

Reactions were performed under a positive pressure of dry argon in oven-dried glassware equipped with a magnetic stir bar. Standard inert atmosphere techniques were used in handling all air and moisture sensitive reagents. THF was freshly distilled from sodium and CH₂Cl₂ from CaH₂. Reactions were monitored by thin layer chromatography (TLC) using commercial aluminum-backed silica gel plates (Merck G 60 F254). TLC spots were viewed under ultraviolet light and by heating the plate after treatment with either a 2% solution of potassium permanganate in 7% aqueous sodium carbonate or a 1% triphenyltetrazolium chloride (TTC) in ethanol. Product purification by gravity column chromatography was performed using Macherey-Nagel Silica Gel 60 (70-230 mesh). Melting points were determined with a Büchi B-545 apparatus. Infrared (IR) spectra were recorded on a Nicolet Magna-550 Fourier transform infrared spectrometer (FTIR) equipped with an ATR (Attenuated Total Reflection) device and the data are reported in reciprocal centimeters (cm⁻¹). ¹H NMR and ¹³C NMR spectra were run on Bruker Advance300 spectrometer. Chemical shifts for ¹H spectra are values downfield from tetramethylsilane in CDCl₃ (δ 0.00) and are reported as follows: chemical shift (ppm), multiplicity, integration, and coupling constants (Hz). Mass spectra (MS) were recorded on a ThermoFinnigan PolarisQ ion-trap spectrometer using a Bruker Esquire 3000 plus (ESI). High resolution mass spectra (HRMS) were recorded on a Thermoquest Orbitrap spectrometer at the LCOSB, UMR 7613, Université Pierre et Marie Curie, Paris.

General procedure for the synthesis of nitrones 1-3

![Reactions](image)

To a stirred suspension of corresponding aldehyde (3.0 mmol) and benzylhydroxylamine (406 mg, 3.3 mmol) in CH₂Cl₂ (10 mL) MgSO₄ (1.08 g, 9.0 mmol) was added at room temperature. After 1 hour of stirring MgSO₄ was filtered off, CH₂Cl₂ was evaporated under reduced pressure. The solid residue was recrystallized from EtOAc to afford corresponding nitrone as white crystals.
(Z)-N-(cyclopropylmethylene)-1-phenylmethanamine oxide 1 (452 mg, 86%) was obtained from cyclopropanecarbaldehyde (210 mg, 3.0 mmol); mp 129-130 °C (EtOAc). IR (neat): 700, 760, 950, 1120, 1220, 1425, 1460, 1605, 3005, 3060 cm⁻¹. ¹H NMR (300 MHz, CDCl₃): δ = 0.60-0.66 (m, 2H), 0.99-1.06 (m, 2H), 2.31-2.43 (m, 1H), 4.85 (s, 2H), 6.08 (d, J = 8.5 Hz, 1H), 7.35-7.40 (m, 5H). ¹³C NMR (75 MHz, CDCl₃): δ = 6.9 (2C), 9.4, 68.7, 128.7, 128.8 (2C), 129.1 (2C), 132.9, 142.0. MS (ES⁺): m/z (%) = 198 (11) [M + Na]^+, 176 (100) [M + H]^+. HRMS: m/z [M + Na]^+ calculated for C₁₁H₁₃NNaO: 198.0889; found: 198.0891.

Trans-(Z)-1-phenyl-N-(2-phenylcyclopropyl)methylene)methanamine oxide 2 (617 mg, 82%) was obtained from trans-2-phenylcyclopropanecarbaldehyde (438 mg, 3.0 mmol); mp 122-123 °C (EtOAc). IR (neat): 695, 745, 935, 955, 1075, 1120, 1460, 1495, 1605, 3030, 3060 cm⁻¹. ¹H NMR (300 MHz, CDCl₃): δ = 1.23-1.29 (m, 1H), 1.40-1.47 (m, 1H), 2.17-2.24 (m, 1H), 2.60-2.70 (m, 1H), 4.86 (s, 2H), 6.24 (d, J = 8.3 Hz, 1H), 7.07-7.26 (m, 5H), 7.36-7.41 (m, 5H). ¹³C NMR (75 MHz, CDCl₃): δ = 16.1, 20.6, 24.7, 68.8, 126.0 (2C), 126.2, 128.3 (2C), 128.8 (3C), 129.3 (2C), 132.7, 139.8, 140.2. MS (ES⁺): m/z (%) = 274 (12) [M + Na]^+, 252 (100) [M + H]^+. HRMS: m/z [M + Na]^+ calculated for C₁₇H₁₇NNaO: 274.1202; found: 274.1202.

(Z)-N-((2,2-diphenylcyclopropyl)methylene)-1-phenylmethanamine oxide 3 (903 mg, 92%) was obtained from 2,2-diphenylcyclopropanecarbaldehyde (666 mg, 3.0 mmol); mp 120-121 °C. IR (neat): 695, 750, 1030, 1125, 1190, 1455, 1495, 1595, 3030, 3075 cm⁻¹. ¹H NMR (300 MHz, CDCl₃): δ = 1.66-1.77 (m, 2H), 3.09-3.17 (m, 1H), 4.73 (s, 2H), 5.92 (d, J = 7.9 Hz, 1H), 7.10-7.36 (m, 15H). ¹³C NMR (75 MHz, CDCl₃): δ = 21.0, 23.6, 39.3, 69.0, 126.5, 126.9, 127.9 (2C), 128.3 (2C), 128.6 (2C), 128.7 (3C), 129.3 (2C), 129.7 (2C), 132.7, 138.9, 140.9, 144.5. MS (ES⁺): m/z (%) = 350 (13) [M + Na]^+, 328 (100) [M + H]^+. HRMS: m/z [M + Na]^+ calculated for C₂₃H₂₁NNaO: 350.1515; found: 350.1513.
General procedure for the coupling reaction between nitrones 1-3 and cyclohexanone

Conditions A. To a stirred and carefully deoxygenated solution of corresponding nitrone 1-3 (0.2 mmol) and cyclohexanone (31 µL, 0.3 mmol) in 5 mL of dry THF, a 0.1 M solution of SmI\(_2\) (4.4 mL, 0.44 mmol) was added at −78 °C under argon. After 3 hour, a saturated solutions of Na\(_2\)S\(_2\)O\(_3\) (5 mL) and NaHCO\(_3\) (5 mL), and EtOAc (20 mL) were added. After extraction the organic phase was washed with brine, dried over Na\(_2\)SO\(_4\), filtered, and concentrated. Column chromatography yielded racemic products 11-13 (eluent: EtOAc-pentane, 1:4) and recovered nitrones 1-3 (eluent: MeOH-EtOAc, 5:95).

Conditions B. To a stirred and carefully deoxygenated solution of corresponding nitrone 1-3 (0.2 mmol) and cyclohexanone (31 µL, 0.3 mmol) in 5 mL of dry THF degassed water (58 µL, 3.2 mmol) was added at −78 °C under argon. Then a 0.1 M solution of SmI\(_2\) (6.0 mL, 0.6 mmol) was added. After 3 hour, a saturated solutions of Na\(_2\)S\(_2\)O\(_3\) (5 mL) and NaHCO\(_3\) (5 mL), and EtOAc (20 mL) were added. After extraction the organic phase was washed with brine, dried over Na\(_2\)SO\(_4\), filtered, and concentrated. Column chromatography using EtOAc-pentane (1:4) yielded racemic products 11-13.

1-((Benzyl(hydroxy)amino)(cyclopropyl)methyl)cyclohexanol 11 (white foam). IR (neat): 690, 740, 960, 1025, 1425, 1440, 2855, 2925, 3300 cm\(^{-1}\). \(^{1}\)H NMR (300 MHz, CDCl\(_3\)): δ = 0.22-0.30 (m, 1H), 0.50-0.68 (m, 2H), 0.73-0.82 (m, 1H), 1.12-1.26 (m, 2H), 1.47-1.79 (m, 9H), 1.90 (d, \(J = 10.4\) Hz, 1H), 3.87 (d, \(J = 13.3\) Hz, 1H), 4.29 (d, \(J = 13.3\) Hz, 1H), 5.12 (br.s, 1H), 7.22-7.35 (m, 5H). \(^{13}\)C NMR (75 MHz, CDCl\(_3\)): δ = 3.3, 3.7, 5.3, 21.8, 22.2, 25.9, 34.1, 36.7, 63.1, 74.3, 78.3, 127.3, 128.3 (2 C), 129.2 (2 C), 138.6. MS (ES\(^{+}\)): \(m/z\) (%) = 276 (100) [M + H]\(^{+}\). HRMS: \(m/z\) [M + H]\(^{+}\) calculated for C\(_{17}\)H\(_{26}\)NO\(_2\): 276.1958; found: 276.1960. Coupling reaction of nitrone 1 (35 mg, 0.2 mmol) and cyclohexanone under conditions A afforded 30 mg (55%) of product 11 and 10 mg (30%) of recovered nitrone 1. Coupling reaction of nitrone 1 (35 mg, 0.2 mmol) and cyclohexanone under conditions B afforded 50 mg (91%) of product 11; the amount of starting nitrone 1 in crude reaction mixture was detected to be 5% by NMR \(^{1}\)H.
**Trans-1-((benzyl(hydroxy)amino)(2-phenylcyclopropyl)methyl)cyclohexanol 12** (colorless oil, 1:3 mixture of two diastereomers). IR (neat): 695, 735, 910, 955, 1030, 1065, 1095, 1450, 1495, 1605, 2855, 2930, 3340 cm\(^{-1}\). \(^1\)H NMR (300 MHz, CDCl\(_3\), major diastereomer): δ = 0.93-0.99 (m, 1H), 1.07-1.14 (m, 1H), 1.18-1.26 (m, 2H), 1.41-1.83 (m, 9H), 2.04-2.10 (m, 1H), 2.17 (d, J = 10.2 Hz, 1H), 3.89 (d, J = 13.3 Hz, 1H), 4.20 (d, J = 13.3 Hz, 1H), 5.13 (br.s, 1H), 7.08-7.38 (m, 10H).

\(^13\)C NMR (75 MHz, CDCl\(_3\)): δ = 14.6, 17.9, 21.8, 22.0, 22.2, 25.9, 34.3, 36.7, 63.0, 74.4, 77.9, 125.7, 126.0 (2C), 127.3, 128.3 (2C), 128.4 (2C), 129.2 (2 C), 138.4, 142.4. MS (ES\(^+\)): m/z (%) = 352 (100) [M + H]\(^+\). HRMS: m/z [M + H]\(^+\) calculated for C\(_{23}\)H\(_{30}\)NO\(_2\): 352.2271; found: 352.2264. Coupling reaction of nitrone 2 (50 mg, 0.2 mmol) and cyclohexanone under conditions A afforded 15 mg (20%) of product 12 (dr 1:2) and 35 mg (70%) of recovered nitrone 2. Coupling reaction of nitrone 2 (50 mg, 0.2 mmol) and cyclohexanone under conditions B afforded 60 mg (86%) of product 12 (dr 1:3).

**1-((benzyl(hydroxy)amino)(2,2-diphenylcyclopropyl)methyl)cyclohexanol 13** (white foam). IR (neat): 695, 755, 970, 1030, 1130, 1265, 1395, 1445, 1495, 1600, 2855, 2930, 3335 cm\(^{-1}\). \(^1\)H NMR (300 MHz, CDCl\(_3\)): δ = 1.12-1.23 (m, 1H), 1.38-1.43 (m, 1H), 1.48-1.87 (m, 10H), 2.34 (d, J = 10.6 Hz, 1H), 2.46-2.55 (m, 1H), 2.62 (d, J = 13.7 Hz, 1H), 3.58 (d, J = 13.7 Hz, 1H), 4.77 (br.s, 1H), 7.10-7.42 (m, 14H), 7.59 (d, J = 7.0 Hz, 1H). \(^13\)C NMR (75 MHz, CDCl\(_3\)): δ = 18.7, 21.8, 22.2, 23.2, 26.0, 33.5, 34.0, 36.9, 63.4, 71.0, 74.2, 125.8, 126.4, 127.1, 127.9 (2C), 128.2 (2C), 128.4 (2C), 128.5 (2C), 129.0 (2 C), 130.6 (2 C), 138.6, 142.6, 146.9. MS (ES\(^+\)): m/z (%) = 428 (100) [M + H]\(^+\). HRMS: m/z [M + H]\(^+\) calculated for C\(_{29}\)H\(_{34}\)NO\(_2\): 428.2584; found: 428.2584. Coupling reaction of nitrone 3 (65 mg, 0.2 mmol) and cyclohexanone under conditions A afforded 30 mg (35%) of product 13 and 40 mg (62%) of recovered nitrone 3. Coupling reaction of nitrone 3 (65 mg, 0.2 mmol) and cyclohexanone under conditions B afforded 70 mg (82%) of product 13.

**SmI\(_2\)-mediated coupling reaction between nitrone 2 and ethyl acrylate**
Conditions A. To a stirred and carefully deoxygenated solution of nitrone 2 (50 mg, 0.2 mmol) and ethyl acrylate (27 µL, 0.25 mmol) in 5 mL of dry THF, a 0.1 M solution of SmI$_2$ (4.4 mL, 0.44 mmol) was added at −78 °C under argon. After 3 hour, a saturated solutions of Na$_2$S$_2$O$_3$ (5 mL) and NaHCO$_3$ (5 mL), and EtOAc (20 mL) were added. After extraction the organic phase was washed with brine, dried over Na$_2$SO$_4$, filtered, and concentrated. Column chromatography yielded 15 mg (20%) of product 14 (dr 1:6) (eluent: EtOAc-pentane, 1:4) and 30 mg (60%) of recovered nitrone 2 (eluent: MeOH-EtOAc, 5:95).

Conditions B. To a stirred and carefully deoxygenated solution of corresponding nitrone 2 (50 mg, 0.2 mmol) and ethyl acrylate (27 µL, 0.25 mmol) in 5 mL of dry THF degassed water (29 µL, 1.6 mmol) was added at −78 °C under argon. Then a 0.1 M solution of SmI$_2$ (6.0 mL, 0.6 mmol) was added. After 3 hour, a saturated solutions of Na$_2$S$_2$O$_3$ (5 mL) and NaHCO$_3$ (5 mL), and EtOAc (20 mL) were added. After extraction the organic phase was washed with brine, dried over Na$_2$SO$_4$, filtered, and concentrated. Column chromatography yielded 60 mg (85%) of product 14 (dr 1:2) (eluent: EtOAc-pentane, 1:4) and 5 mg (10%) of recovered nitrone 2 (eluent: MeOH-EtOAc, 5:95).

Ethyl trans-4-(benzyl(hydroxy)amino)-4-(2-phenylcyclopropyl)butanoate 14 (colorless oil, 1:6 mixture of two diastereomers). IR (neat): 695, 750, 1030, 1145, 1180, 1375, 1455, 1495, 1605, 1730, 2925, 2980, 3470 cm$^{-1}$. $^1$H NMR (300 MHz, CDCl$_3$, major diastereomer): $\delta$ = 0.69-0.76 (m, 1H), 0.93-0.99 (m, 1H), 1.28 (t, $J$ = 7.1 Hz, 3H), 1.43-1.52 (m, 1H), 1.81-1.96 (m, 2H), 2.06-2.25 (m, 2H), 2.32-2.54 (m, 2H), 3.83 (d, $J$ = 13.4 Hz, 1H), 4.10 (dq, $J_1$ = 7.1 Hz, $J_2$ = 2.0 Hz 1H), 4.12 (d, $J$ = 13.4 Hz, 1H), 5.36 (br.s, 1H), 7.09-7.33 (m, 10H). $^{13}$C NMR (75 MHz, CDCl$_3$): $\delta$ = 12.7, 14.1, 21.8, 24.5, 26.6, 31.9, 60.6 (2C), 70.4, 125.6, 125.7 (2C), 126.9, 128.1 (2C), 128.4 (2C), 128.8 (2 C), 138.8, 142.3, 175.3. MS (ES$^+$): $m/z$ (%) = 354 (100) [M + H]$^+$. HRMS: $m/z$ [M + H]$^+$ calculated for C$_{22}$H$_{38}$NO$_3$: 354.2064; found: 354.2059.

SmI$_2$-mediated reaction between nitrone 1 and water

To a stirred and carefully deoxygenated solution of nitrone 1 (53 mg, 0.3 mmol) in 5 mL of dry THF degassed water (86 µL, 4.8 mmol) was added at −78 °C under argon. Then a 0.1 M
solution of SmI$_2$ (9.0 mL, 0.9 mmol) was added. After 3 hour, a saturated solutions of Na$_2$S$_2$O$_3$ (5 mL) and NaHCO$_3$ (5 mL), and EtOAc (20 mL) were added. After extraction the organic phase was washed with brine, dried over Na$_2$SO$_4$, filtered, and concentrated. Column chromatography yielded 15 mg (28%) of product 15 (eluent: EtOAc-pentane, 1:4) and 20 mg (40%) of recovered nitrone 1 (eluent: MeOH-EtOAc, 1:9).

**N-benzyl-N-(cyclopropylmethyl)hydroxylamine 15** (colorless oil). IR (neat): 700, 750, 830, 1010, 1100, 1270, 1325, 1455, 2835, 3005, 3190 cm$^{-1}$. $^1$H NMR (300 MHz, CDCl$_3$): $\delta = 0.04$-0.09 (m, 2H), 0.38-0.44 (m, 2H), 0.84-.97 (m, 1H), 2.45 (d, $J = 6.8$ Hz, 2H), 3.72 (s, 2H), 7.16-7.27 (m, 5H). $^{13}$C NMR (75 MHz, CDCl$_3$): $\delta = 3.8$ (2C), 8.5, 64.2, 64.6, 127.4, 128.2 (2 C), 129.8 (2 C), 137.2. MS (ES$^+$): $m/z$ (%) = 178 (100) [M + H]$^+$. HRMS: $m/z$ [M + H]$^+$ calculated for C$_{11}$H$_{16}$NO: 178.1226; found: 178.1225.

**SmI$_2$-mediated reaction between nitrone 2 and water**

To a stirred and carefully deoxygenated solution of nitrone 2 (100 mg, 0.4 mmol) in 5 mL of dry THF degassed water (115 µL, 6.4 mmol) was added at −78 °C under argon. Then a 0.1 M solution of SmI$_2$ (12.0 mL, 1.2 mmol) was added. After 3 hour, a saturated solutions of Na$_2$S$_2$O$_3$ (5 mL) and NaHCO$_3$ (5 mL), and EtOAc (20 mL) were added. After extraction the organic phase was washed with brine, dried over Na$_2$SO$_4$, filtered, and concentrated. Column chromatography yielded 15 mg (15%) of product 16 (eluent: EtOAc-pentane, 1:4) and 35 mg (35%) of nitrone 17 (eluent: MeOH-EtOAc, 1:9).

**Trans-N-benzyl-N-((2-phenylcyclopropyl)methyl)hydroxylamine 16** (colorless oil). IR (neat): 700, 740, 1030, 1265, 1455, 1495, 1605, 2855, 2925, 3030, 3060, 3250 cm$^{-1}$. $^1$H NMR (300 MHz, CDCl$_3$): $\delta = 0.82$-0.98 (m, 2H), 1.26-1.41 (m, 1H), 1.71-1.77 (m, 1H), 2.63-2.77 (m, 2H), 3.79 (s, 2H), 7.03-7.41 (m, 10H). $^{13}$C NMR (75 MHz, CDCl$_3$): $\delta = 14.7$, 20.9, 22.4, 63.9, 64.3, 125.5, 125.7 (2C), 127.3, 128.3 (4C), 129.6 (2C), 137.4, 142.9. MS (ES$^+$): $m/z$ (%) = 254 (100) [M + H]$^+$. HRMS: $m/z$ [M + H]$^+$ calculated for C$_{17}$H$_{20}$NO: 254.1539; found: 254.1539.
(Z)-1-phenyl-N-(4-phenylbutylidene) methanamine oxide 17 (yellow oil). IR (neat): 700, 735, 1030, 1265, 1455, 1495, 1600, 2925, 3025 cm⁻¹. ¹H NMR (300 MHz, CDCl₃): δ = 1.76-1.86 (m, 2H), 2.48-2.55 (m, 2H), 2.63 (t, J = 7.8 Hz, 2H), 4.82 (s, 2H), 6.55 (t, J = 5.8 Hz, 1H), 7.12-7.36 (m, 10H). ¹³C NMR (75 MHz, CDCl₃): δ = 26.3, 27.1, 35.6, 69.1, 126.0, 128.3 (3C), 128.9 (4C), 129.2 (2C), 132.8, 141.3 (2C). MS (ES⁺): m/z (%) = 276 (10) [M + Na]⁺, 254 (100) [M + H]⁺. HRMS: m/z [M + Na]⁺ calculated for C₁₇H₁₉NNaO: 276.1359; found: 276.1361.

SmI₂-mediated reaction between nitrone 3 and water

To a stirred and carefully deoxygenated solution of nitrone 3 (65 mg, 0.2 mmol) in 5 mL of dry THF degassed water (58 µL, 3.2 mmol) was added at −78 °C under argon. Then a 0.1 M solution of SmI₂ (6.0 mL, 0.6 mmol) was added. After 3 hour, a saturated solutions of Na₂S₂O₃ (5 mL) and NaHCO₃ (5 mL), and EtOAc (20 mL) were added. After extraction the organic phase was washed with brine, dried over Na₂SO₄, filtered, and concentrated. Column chromatography yielded 23 mg (35%) of nitrone 18 (elucent: MeOH-EtOAc, 1:9).

(Z)-N-(4,4-diphenylbutylidene)-1-phenylmethanamine oxide 18 (yellow oil). IR (neat): 695, 735, 915, 1030, 1155, 1265, 1450, 1495, 1600, 2925, 3025, 3060 cm⁻¹. ¹H NMR (300 MHz, CDCl₃): δ = 2.20-2.28 (m, 2H), 2.42-2.49 (m, 2H), 3.86 (t, J = 7.8 Hz, 1H), 4.77 (s, 2H), 6.49 (t, J = 5.8 Hz, 1H), 7.13-7.38 (m, 15H). ¹³C NMR (75 MHz, CDCl₃): δ = 25.7, 31.1, 51.3, 69.0, 126.1, 126.4 (2C), 127.7 (4C), 128.5 (4C), 128.9 (2C), 129.7 (2 C), 132.7, 139.1, 144.1 (2C). MS (ES⁺): m/z (%) = 352 (20) [M + Na]⁺, 330 (100) [M + H]⁺. HRMS: m/z [M + Na]⁺ calculated for C₂₃H₂₃NNaO: 352.1672; found: 352.1671.