Supporting Information Available

Synthesis of 2,3-Dihydro-isoxazoles from Propargylic *N*-Hydroxylamines: Ring Closure Reaction Catalyzed by Zn(II)

(cover & 11 pages)

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Tools, Reagents, Solvents and Procedures

IR-Spectra were recorded on a *Perkin Elmer Spectrum RX I FT-IR spectraphotometer*. The samples were prepared as either KBr pellets or thin films on NaCl salt plates and are reported as absorption maxima in cm^{-1} with corresponding characteristic intensity (*s* = strong, *m* = medium, *w* = weak).

^{1}H-NMR-Spectra were recorded on a *Varian Mercury 300* operating at 300 MHz or a *Gemini 200* operating at 200 MHz. Chemical shifts δ (ppm) were referenced to the internal solvent signals. Multiplicities are declared as follows: *s* (singlet), *d* (doublet), *t* (triplet), *sep* (septet) and *m* (multiplet). Coupling constants *J* are given in Hz.

^{13}C-NMR-Spectra were recorded on a *Varian Mercury 300* operating at 75 MHz. Chemical shifts δ (ppm) were referenced to the internal solvent signals.

Melting points were measured using a *Büchi 510* melting point apparatus and are uncorrected.

Elemental analysis was performed by the Mikroelementaranalytisches Laboratorium at the ETH, Zürich. Calculated and observed data are given in mass percent.

TLC: Thin layer chromatography was performed using *Merck Silica Gel 60 F_{254} TLC plates* and visualized either with ultraviolet light at 254 nm, stained iodine or by a solution of 5 g $NaHCO_3$, 1.5 g $KMnO_4$ and 400 ml H_2O or 25 g phosphor molybdic acid, 10 g $Ce(SO_4)_2 \cdot H_2O$, 60 ml conc. H_2SO_4 and 940 ml H_2O.

Chromatographic purification of products was accomplished using forced flow chromatography on *Fluka Silica Gel 60* (40 - 63 μm) according to the method of Still [1].

Solvents were all purchased from either Aldrich or Fluka chemical companies and used without prior purification. For chromatic purification, solvents were distillated prior to use.

Reactions: Reactions were all performed using oven dried glassware under an atmosphere of dry nitrogen or argon. Solvents and chemicals were transferred by syringe. Reactions were monitored by TLC. All chiral compounds were obtained in racemic form. ZnI_2 (>99.998%) and $Zn(OTf)_2$ (>99.998%) were used unless otherwise noted.

Preparation of the Hydroxylamines

Preparation of Benzaldehyde Oxime [2]

To a solution of benzaldehyde (31.8 g, 0.300 mol) and hydroxylamine hydrochloride (64.5 g, 1.00 mol) in 1000 ml 90% EtOH was added powdered NaOH (108 g, 2.70 mol) in small portions. The mixture was allowed to stir at 25 °C for 30 min and then refluxed for another 30 min The reaction mixture was then cooled to 25 °C, poured into a mixture of concentrated HCl (120 ml) and water (460 ml), carefully concentrated to one third of the original volume and finally extracted with CH_2Cl_2. The organic layer was washed with brine, dried over $MgSO_4$ and concentrated in *vacuo*. The obtained yellow oil was purified by micro distillation (0.5 torr, bp.: 71°C) to give 32.6 g (90%) benzaldehyde oxime as a colorless oil.

Reduction of the Benzaldehyde Oxime

Reduction with $NaBH_3CN$ [2]

To a solution of benzaldehyde oxime (2.00 g, 16.5 mmol) in MeOH were added $NaBH_3CN$ (1.80 g, 28.0 mmol) and a trace of methyl orange. 12 N HCl was added drop wise until the color remained pink. The reaction mixture was allowed to stir at 25 °C for 3.5 h. After completion the reaction mixture was concentrated in *vacuo* and 6 N NaOH was added until pH ~10. The product was extracted with CH_2Cl_2, washed with brine, dried over anhydrous $MgSO_4$ and concentrated in *vacuo*. The obtained *N*-benzyl-hydroxylamine 1.90 g (94%) was used for the preparation of the nitrones without further purification. The analytical data correlated with the literature [3].

Reduction with Pyridine-Borane [3]

A mixture of the oxime (18.2 g, 150 mmol) and 8 M pyridine-borane (37.5 ml, 300 mmol) in 120 ml EtOH was kept below 5 °C. To this solution, 10% aqueous HCl (240 ml) was added drop wise. The mixture was then warmed up within 30 min to 23°C. The solution was neutralized with sodium carbonate at 0 °C, and extracted with CH_2Cl_2. The combined organic layers were dried over anhydrous Na_2SO_4 and concentrated in *vacuo*. The obtained *N*-benzyl-hydroxylamine 16.6 g (91%) was used for the preparation of the nitrones without further purification. The analytical data correlated with the literature [3].

Preparation of the Nitrones [4]

General Procedure

To a well-stirred solution of 1 eq *N*-benzyl-hydroxylamine and 1eq anhydrous $MgSO_4$ in either dichloromethane or ether, 1 eq aldehyde was added drop wise. Reactions were monitored by TLC. The mixture was filtered and the filtrate concentrated in vacuo to yield the crude product, which was chromatographed on silica gel (ethyl acetate/hexane, 95:5) to afford the pure nitrones.

(Z)-*N*-(2-Methylpropylidene)benzylamine-*N*-oxide

N-benzyl-hydroxylamine (4.92 g, 40.0 mmol), 2-methyl-propionaldehyde (2.88 g, 40.0 mmol) and $MgSO_4$ (4.81 g, 40.0 mmol) were stirred in 300 ml ether for 15 h. Purification using chromatography on silica gel afforded 5.49 g (78%) (Z)-*N*-(2-methylpropylidene)benzylamine-*N*-oxide. The analytical data correlated with the literature [4].

(Z)-*N*-(2,2-Dimethylpropylidene)benzylamine-*N*-oxide

N-benzyl-hydroxylamine (4.92 g, 40.0 mmol), 2,2-dimethyl-propionaldehyde (3.45 g, 40.0 mmol) and $MgSO_4$ (4.81 g, 40.0 mmol) were stirred in 300 ml ether for 15 h. Purification using chromatography on silica gel afforded 6.42 g (84%) (Z)-*N*-(2,2-dimethylpropylidene)-benzylamine-*N*-oxide. The analytical data correlated with the literature [4].

(Z)-*N*-Benzylidene-benzylamine-*N*-oxide

N-benzyl-hydroxylamine (6.16 g, 50.0 mmol), benzaldehyde (5.31 g, 50.0 mmol) and $MgSO_4$ (6.02 g, 50.0 mmol) were stirred in 400 ml CH_2Cl_2 for 15 h. Purification using chromatography on silica gel afforded 9.74 g (92%) (Z)-*N*-benzylidene-benzylamine-*N*-oxid. The analytical data correlated with the literature [4].

Preparation of the Hydroxylamines [5]

General Procedure

A flask was charged with $Zn(OTf)_2$ and purged with nitrogen for 15 min To the flask was added 10 ml CH_2Cl_2, 1.5 eq acetylene and Hünig's base. The resulting mixture was stirred at 23°C for 20 min 1 eq nitrone was dissolved in 10 ml CH_2Cl_2 and added to the flask in one portion. Upon completion, the reaction was quenched by the addition of a saturated aqueous NH_4Cl solution. The reaction mixture was poured into a separatory funnel containing CH_2Cl_2. The layers were separated and the aqueous layer was extracted with CH_2Cl_2. The combined organic layers were washed with brine and dried over $MgSO_4$ and concentrated in *vacuo*. Purification of the crude material by chromatography on silica gel afforded the propargyl hydroxylamine.

***N*-Benzyl-*N*-(1-isopropyl-5-phenyl-pent-2-ynyl)-hydroxylamine**

A solution of 4-phenyl-1-butyne (0.98 g, 7.5 mmol), (Z)-*N*-(2-methylpropylidene)-benzylamine-*N*-oxide (0.89 g, 5.0 mmol), $Zn(OTf)_2$ (0.18 g, 0.50 mmol, 10 mol%) and Hünig's base (0.16 g, 1.2 mmol) was stirred in CH_2Cl_2 for 4 h at 23°C. Purification using chromatography on silica gel (hexane/ethyl acetate, 95:5) afforded 1.4 g (93%) of the title compound as a white solid. The analytical data correlated with the literature [5].

***N*-Benzyl-*N*-[4-(*tert*-butyl-dimethyl-silanyloxy)-1-isopropyl-but-2-ynyl)-hydroxylamine**

A solution of 3-(*tert*-butyl-dimethyl-silanyloxy)-1-butyne [6] (1.28 g, 7.50 mmol), (Z)-*N*-(2-methyl-propylidene)benzylamine-*N*-oxide (0.89 g, 5.0 mmol), $Zn(OTf)_2$ (0.18 g, 0.50 mmol, 10 mol%) and Hünig's base (0.16 g, 1.2 mmol) was stirred in CH_2Cl_2 for 8 h at 23°C. Purification using chromatography on silica gel (hexane/ethyl acetate, 95:5) afforded 1.5 g (88%) of the title compound as colorless crystals. The analytical data correlated with the literature [5].

***N*-Benzyl-*N*-(1-isopropyl-3-phenyl-prop-2-ynyl)-hydroxylamine**

A solution of phenyl acetylene (0.77 g, 7.5 mmol), (Z)-*N*-(2-methylpropylidene)benzylamine-*N*-oxide (0.89 g, 5.0 mmol), $Zn(OTf)_2$ (0.18 g, 0.50 mmol, 10 mol%) and Hünig's base (0.16 g, 1.2 mmol) was stirred in CH_2Cl_2 for 1 h at 23°C. Purification using chromatography on silica gel (hexane/ethyl acetate, 95:5) afforded 1.2 g (90%) of the title compound as a yellowish solid. The analytical data correlated with the literature [5].

***N*-Benzyl-*N*-(1-*tert*-butyl-5-phenyl-pent-2-ynyl)-hydroxylamine**

A solution of 4-phenyl-1-butyne (0.98 g, 7.5 mmol), (Z)-*N*-(2,2-dimethylpropylidene)-benzylamine-*N*-oxide (0.96 g, 5.0 mmol), $Zn(OTf)_2$ (0.18 g, 0.50 mmol, 10 mol%) and Hünig's base (0.16 g, 1.2 mmol) was stirred in CH_2Cl_2 for 6 h at 23°C. Purification using chromatography on silica gel (hexane/methylene chloride, 1:1) afforded 1.5 g (91%) of the title compound as a colorless oil.

^{1}H-NMR (300 MHz, $CDCl_3$) δ: 7.36-7.20 (*m*, 10H), 3.98 (*s*, OH), 3.95 and 3.63 (*2d*, AB, 2H, J_{AB} = 12.8 Hz), 3.14 (*t*, 1H, J = 2 Hz), 2.92 (*t*, 2H, J = 7.3 Hz), 2.71-2.65 (*m*, 2H), 0.95 (*s*, 9H). ^{13}C-NMR (75 MHz, $CDCl_3$)

δ_140.5 (C), 137.5 (C), 129.2 (CH), 128.5 (2CH), 128.3 (CH), 127.3 (CH), 126.4 (CH), 88.8 (C), 74.1 (C), 68.1 (CH), 64.5 (CH_2), 35.3 (CH_2), 35.2 (C), 27.5 (CH_3), 20.7 (CH_2). IR ($CHCl_3$): 3538*m*, 3465*m*, 3379*m*, 3028*s*, 2952*s*, 2865*s*, 2213*w*, 1947*w*, 1873*w*, 1807*w*, 1603*m*, 1454*s*, 1363*s*, 745*s*, 698*s*. Anal. Calcd. for $C_{22}H_{27}NO$ (321.46): C, 82.20; H, 8.47; N, 4.36. Found: C, 82.16; H, 8.41; N, 4.35.

_N_-Benzyl-_N_-[4-(*tert*-butyl-dimethyl-silanyloxy)-1-(dimethyl-ethyl)-but-2-ynyl]-hydroxylamine

A solution of 3-(*tert*-butyl-dimethyl-silanyloxy)-1-butyne (1.28 g, 7.50 mmol), (Z)-*N*-(2,2-dimethyl-propylidene)benzylamine-*N*-oxide (0.96 g, 5.0 mmol), $Zn(OTf)_2$ (0.18 g, 0.50 mmol, 10 mol%) and Hünig's base (0.16 g, 1.2 mmol) was stirred in CH_2Cl_2 for 7 h at 23°C. Purification using chromatography on silica gel (hexane/methylene chloride, 1:1) afforded 1.6 g (89%) of the title compound as a yellowish oil.

^{1}H-NMR (300 MHz, $CDCl_3$) δ: 7.40-7.25 (*m*, 5H), 4.48 (*d*, 2H, J = 1.9 Hz), 4.25 (*s*, OH), 4.10 and 3.80 (*2d*, AB, 2H, J_{AB} = 12.8 Hz), 3.27 (*t*, 1H, J = 1.9 Hz), 1.02 (*s*, 9H), 0.96 (*s*, 9H), 0.18 (*s*, 6H). ^{13}C-NMR (75 MHz, $CDCl_3$) δ: 137.5 (C), 129.3 (CH), 128.4 (CH), 127.4 (CH), 87.8 (C), 78.6 (C), 68.1 (CH), 64.5 (CH_2), 51.8 (CH_2), 35.4 (C), 27.7 (CH_3), 25.8 (CH_3), 18.3 (C), -5.0 (CH_3). IR ($CHCl_3$): 3455*m*, 2955*s*, 2930*s*, 2859*s*, 1947*w*, 1808*w*, 1605*w*, 1462*m*, 1365*m*, 1255*m*, 1126*s*, 1082*s*, 837*s*, 779*s*, 700*m*. Anal. Calcd. for $C_{21}H_{35}SiNO_2$ (361.60): C, 69.75; H, 9.76; N, 3.87. Found: C, 69.86; H, 9.55; N, 4.08.

_N_-Benzyl-_N_-(1-*tert*-butyl-3-phenyl-prop-2-ynyl)-hydroxylamine

A solution of phenyl acetylene (0.77 g, 7.5 mmol), (Z)-*N*-(2,2-dimethyl-propylidene)-benzylamine-*N*-oxide (0.96 g, 5.0 mmol), $Zn(OTf)_2$ (0.18 g, 0.50 mmol, 10 mol%) and Hünig's base (0.16 g, 1.2 mmol) was stirred in CH_2Cl_2 for 1 h at 23°C. Purification using chromatography on silica gel (hexane/methylene chloride, 1:1) afforded 1.4 g (94%) of the title compound as a white solid.

^{1}H-NMR (300 MHz, $CDCl_3$) δ: 7.55-7.26 (*m*, 10H), 4.29 (*s*, OH), 4.18 and 3.90 (*2d*, AB, 2H, J_{AB} = 12.8 Hz), 3.46 (*s*, 1H), 1.10 (*s*, 9H). ^{13}C-NMR (75 MHz, $CDCl_3$) δ: 137.5 (C), 131.9 (CH), 129.3 (CH), 128.4 (CH), 128.3 (CH), 128.3 (CH), 127.5 (CH), 122.9 (C), 89.3 (C), 93.4 (C), 68.6 (CH), 64.6 (CH_2), 35.7 (C), 27.7 (CH_3). IR ($CHCl_3$): 3537*m*, 3462*m* 2954*s*, 2867*m* 1950*w*, 1882*w*, 1810*w*, 1598*m*, 1490*s*, 1455*m*, 1393*m*, 1365*m*, 1220*m*, 772*s*, 692*s*. Anal. Calcd. for $C_{20}H_{23}NO$ (293.41): C, 81.87; H, 7.90; N, 4.77. Found: C, 82.08; H, 7.93; N, 4.73. mp: 74-76°C.

_N_-Benzyl-_N_-(1,5-diphenyl-pent-2-ynyl)-hydroxylamine

A solution of 4-phenyl-1-butyne (0.98 g, 7.5 mmol), (Z)-*N*-benzylidene-benzylamine-*N*-oxide (1.06 g, 5.00 mmol), $Zn(OTf)_2$ (1.82 g, 5.00 mmol) and Hünig's base (0.65 g, 5.0 mmol) was stirred in CH_2Cl_2 for 18 h at 23°C. Purification using chromatography on silica gel (hexane/methylene chloride, 1:1) afforded 1.4 g (82%) of the title compound as a white solid.

^{1}H-NMR (300 MHz, $CDCl_3$) δ: 7.50-7.21 (*m*, 15H), 5.01 (*s*, OH), 4.70 (*s*, 1H), 3.84 and 3.77 (*2d*, AB, 2H, J_{AB} = 13.1 Hz), 2.96 (*t*, 2H, J = 7.3 Hz), 2.76-2.70 (*m*, 2H). ^{13}C-NMR (75 MHz, $CDCl_3$) δ: 140.6 (C), 137.9 (C), 137.5 (C), 129.5 (CH), 128.7 (CH), 128.6 (CH), 128.5 (CH), 128.3 (CH), 128.2 (CH), 127.8 (CH), 127.4

(CH), 126.4 (CH), 88.6 (C), 75.6 (C), 62.8 (CH_2), 60.0 (CH), 35.1 (CH_2), 21.0 (CH_2). IR ($CHCl_3$): 3531*w*, 3234*m*, 3029*m*, 2908*m*, 1951*w*, 1885*w*, 1810*w*, 1603*m*, 1603*m*, 1495*s*, 1454*s*, 1339*m*, 1220*m*, 1076*m*, 1030*m*, 772*s*, 698*s*. Anal. Calcd. for $C_{24}H_{23}NO$ (341.45): C, 84.42; H, 6.79; N, 4.10. Found: C, 84.23; H, 6.92; N, 4.13. mp: 73-75°C.

_N_-Benzyl-_N_-[4-(*tert*-butyl-dimethyl-silanyloxy)-1-phenyl-but-2-ynyl]-hydroxylamine

A solution of 3-(*tert*-butyl-dimethyl-silanyloxy)-1-butyne (1.28 g, 7.50 mmol), (Z)-*N*-benzylidene-benzylamine-*N*-oxide (1.06 g, 5.00 mmol), $Zn(OTf)_2$ (1.82 g, 5.00 mmol) and Hünig's base (0.65 g, 5.0 mmol) was stirred in CH_2Cl_2 for 18 h at 23°. Purification using chromatography on silica gel (hexane/methylene chloride, 1:1) afforded 1.4 g (68%) of the title compound as a yellowish solid.

^{1}H-NMR (300 MHz, $CDCl_3$) δ: 7.59-7.26 (*m*, 10H), 4.88 (*s*, OH), 4.81 (*s*, 1H), 4.52 (*d*, 2H, J = 1.9 Hz), 4.00 and 3.92 (*2d*, AB, 2H, J_{AB} = 12.8 Hz), 0.94 (*s*, 9H), 0.17 (*s*, 6H). ^{13}C-NMR (75 MHz, $CDCl_3$) δ: 137.5 (C), 137.4 (C), 129.5 (CH), 128.8 (CH), 128.3 (CH), 128.3 (CH), 128.0 (CH), 127.4 (CH), 87.4 (C), 79.9 (C), 62.8 (CH_2), 60.6 (CH), 51.9 (CH_2), 25.8 (CH_3), 18.3 (C), -5.1 (CH_3). IR ($CHCl_3$): 3237*m*, 3032*m*, 2929*s*, 2857*s*, 1952*w*, 1895*w*, 1812*w*, 1454*m*, 1368*m*, 1288*m*, 1220*m*, 1128*m*, 1084*s*, 1003*w*, 836*s*, 775*s*, 699*s*. Anal. Calcd. for $C_{23}H_{31}SiNO_2$ (381.59): C, 72.40; H, 8.19; N, 3.67. Found: C, 72.43; H, 8.20; N, 3.69. mp: 80-82°C.

_N_-Benzyl-_N_-(1,3-diphenyl-prop-2-ynyl)-hydroxylamine

A solution of phenylacetylene (0.77 g, 7.5 mmol), (Z)-*N*-benzylidene-benzylamine-*N*-oxide (1.06 g, 5.00 mmol), $Zn(OTf)_2$ (1.82 g, 5.00 mmol) and Hünig's base (0.65 g, 5.0 mmol) was stirred in CH_2Cl_2 for 18 h at 23°C. Purification using chromatography on silica gel (hexane/methylene chloride, 1:1) afforded 1.4 g (92%) of the title compound as a white solid.

^{1}H-NMR (300 MHz, $CDCl_3$) δ: 7.64-7.26 (*m*, 15H), 5.80 (*s*, OH), 4.88 (*s*, 1H), 4.01 and 3.90 (*2d*, AB, 2H, J_{AB} = 12.9 Hz). ^{13}C-NMR (75 MHz, $CDCl_3$) δ: 137.6 (C), 137.3 (C), 132.0 (CH), 129.7 (CH), 129.0 (CH), 128.5 (CH), 128.4 (CH), 128.4 (CH), 128.1(CH), 127.5 (CH), 122.9 (C), 88.8 (C), 84.7 (C), 63.2 (CH_2), 60.6 (CH). IR ($CHCl_3$): 3529*w*, 3234*m*, 3063*m*, 3031*m*, 2907*m*, 1953*w*, 1883*w*, 1811*w*, 1598*m*, 1490*s*, 1454*s*, 1336*m*, 1219*m*, 1028*m*, 756*s*, 698*s*. Anal. Calcd. for $C_{22}H_{19}NO$ (313.40): C, 84.32; H, 6.11; N, 4.47. Found: C, 84.35; H, 6.16; N, 4.53. mp: 134-136°C.

Catalytic Cyclizations

General Procedure

A flask was charged with 0.1 eq zinc salt and purged with nitrogen for 15 min To the flask was added a solution of 1 eq hydroxylamine in 2 ml CH_2Cl_2. The resulting mixture was stirred at 23°C for 10 min 0.1 eq DMAP was dissolved in 1 ml CH_2Cl_2 and added to the flask in one portion. Upon completion, the reaction was quenched by the addition of 2 ml saturated aqueous NH_4Cl solution. The reaction mixture was poured into a separatory funnel containing 10 ml CH_2Cl_2. The layers were separated and the aqueous layer was extracted with CH_2Cl_2 (3 x 10 ml). The combined organic layers were washed with brine, dried over $MgSO_4$ and concentrated in *vacuo*.

Cyclization with various Zinc Salts

Cyclization with ZnI_2 (purum, >98%)

N-benzyl-*N*-(1-isopropyl-5-phenyl-pent-2-ynyl)-hydroxylamine (150 mg, 0.500 mmol), ZnI_2 (16 mg, 0.050 mmol, 10 mol%), and DMAP (6 mg, 0.05 mmol, 10 mol%) were stirred for 1.5 h at 23°C. Workup and purification using chromatography on silica gel (methylene chloride/hexane, 6:4) afforded 143 mg (93%) 2-benzyl-3-isopropyl-5-phenethyl-2,3-dihydro-isoxazole as a colorless oil.

Cyclization with $ZnBr_2$ (purum, >98%)

N-benzyl-*N*-(1-isopropyl-5-phenyl-pent-2-ynyl)-hydroxylamine (154 mg, 0.500 mmol), $ZnBr_2$ (11 mg, 0.050 mmol, 10 mol%), and DMAP (6 mg, 0.05 mmol, 10 mol%) were stirred for 8 h at 23°C. Workup and purification using chromatography on silica gel (methylene chloride/hexane, 6:4) afforded 140 mg (91%) 2-benzyl-3-isopropyl-5-phenethyl-2,3-dihydro-isoxazole as a colorless oil.

Cyclization with $ZnCl_2$ (purum, >98%)

N-benzyl-*N*-(1-isopropyl-5-phenyl-pent-2-ynyl)-hydroxylamine (154 mg, 0.500 mmol), $ZnCl_2$ (7 mg, 0.05 mmol, 10 mol%), and DMAP (6 mg, 0.05 mmol, 10 mol%) were stirred for 14 h at 23°C. Workup and purification using chromatography on silica gel (methylene chloride/hexane, 6:4) afforded 144 mg (93%) 2-benzyl-3-isopropyl-5-phenethyl-2,3-dihydro-isoxazole as a colorless oil.

Cyclization with $Zn(OTf)_2$

N-benzyl-*N*-(1-isopropyl-5-phenyl-pent-2-ynyl)-hydroxylamine (154 mg, 0.500 mmol), $Zn(OTf)_2$ (18 mg, 0.05 mmol, 10 mol%), and DMAP (6 mg, 0.05 mmol, 10 mol%) were stirred for 72 h at 23°C to afford 100% recovered starting material.

Cyclization to the Δ^4-Isoxazolines

2-Benzyl-3-isopropyl-5-phenethyl-2,3-dihydro-isoxazole

N-benzyl-*N*-(1-isopropyl-5-phenyl-pent-2-ynyl)-hydroxylamine (154 mg, 0.500 mmol), ZnI_2 (16 mg, 0.050 mmol, 10 mol%), and DMAP (6 mg, 0.05 mmol, 10 mol%) were stirred for 1 h at 23°C. Workup and purification using chromatography on silica gel (methylene chloride/hexane, 6:4) afforded 145 mg (95%) of the title compound as a colorless oil.

^{1}H-NMR (300 MHz, $CDCl_3$) δ: 7.41-7.17 (*m*, 10H), 4.52-4.50 (*m*, 1 Vinyl-H), 4.13 and 3.76 (*2d*, AB, 2H, J_{AB} = 12.9 Hz), 3.48-3.44 (*m*, 1H), 2.84 (*t*, 2H, J = 7.9 Hz), 2.51-2.18 (*m*, 2H), 1.59-1.50 (*m*, 1H), 0.78 (*t*, 6H, J = 6.4). ^{13}C-NMR (75 MHz, $CDCl_3$) δ: 154.1 (C), 141.1 (C), 137.1 (C), 129.6 (CH), 128.4 (CH), 128.3 (CH), 128.2 (CH), 127.4 (CH), 126.1(CH), 93.2 (CH), 76.1 (CH), 64.0 (CH_2), 33.8 (CH_2), 33.2 (CH_2), 27.8 (CH), 18.6 (CH_3), 18.2 (CH_3). IR ($CHCl_3$): 3063*w*, 3028*m*, 2956*s*, 2868*m*, 1950*w*, 1877*w*, 1809*w*, 1676*m*, 1604*w*, 1496*m*, 1454*s*, 1362*m*, 1074*m*, 1029*m*, 913*s*, 744*s*. Anal. Calcd. for $C_{21}H_{25}NO$ (307.43): C, 82.04; H, 8.20; N, 4.56. Found: C, 82.16; H, 8.31; N, 4.55.

2-Benzyl-5-(*tert*-butyl-dimethyl-silanyloxymethyl)-3-isopropyl-2,3-dihydro-isoxazole

N-benzyl-*N*-[4-(*tert*-butyl-dimethyl-silanyloxy)-1-isopropyl-but-2-ynyl]-hydroxylamine (174 mg, 0.500 mmol), ZnI_2 (16 mg, 0.050 mmol, 10 mol%), and DMAP (6 mg, 0.05 mmol, 10 mol%) were stirred for 26 h at 23°C. Workup and purification using chromatography on silica gel (methylene chloride/hexane, 6:4) afforded 164 mg (94%) of the title compound as a colorless oil.

^{1}H-NMR (300 MHz, $CDCl_3$) δ: 7.41-7.24 (*m*, 5H), 4.79-4.78 (*m*, 1 Vinyl-H), 4.20 (*s*, 2H), 4.17 and 3.79 (*2d*, AB, 2H, J_{AB} = 12.8 Hz), 3.53-3.49 (*m*, 1H), 1.62-1.53 (*m*, 1H), 0.92 (*s*, 9H), 0.81 (*d*, 6H, J = 6.9 Hz), 0.09 (*s*, 6H). ^{13}C-NMR (75 MHz, $CDCl_3$) δ: 154.1 (C), 136.9 (C), 129.7 (CH), 128.2 (CH), 127.4 (CH), 94.3 (CH), 75.9 (CH_2), 63.9 (CH), 57.4 (CH_2), 33.7 (CH), 25.8 (CH_3), 18.6 (CH_3), 18.4 (C), 18.2 (CH_3). IR ($CHCl_3$): 3031*m*, 2956*s,* 2930*s,* 2858*s,* 1946*w*, 1872*w*, 1809*w*, 1649*m*, 1462*m*, 1256*s,* 1115*s,* 1006*m*, 937*m*, 839*s,* 778*s,* 731*s*, 697*m*. Anal. Calcd. for $C_{20}H_{33}SiNO_2$ (307.43): C, 69.11; H, 9.57; N, 4.03. Found: C, 69.24; H, 9.48; N, 4.23.

2-Benzyl-3-*tert*-butyl-5-phenethyl-2,3-dihydro-isoxazole

N-benzyl-*N*-(1-isopropyl-3-phenyl-prop-2-ynyl)-hydroxylamine (140 mg, 0.500 mmol), ZnI_2 (16 mg, 0.050 mmol, 10 mol%), and DMAP (6 mg, 0.05 mmol, 10 mol%) were stirred for 3 h at 23°C. Workup and purification using chromatography on silica gel (methylene chloride/hexane, 6:4) afforded 132 mg (94%) of the title compound as a colorless oil.

^{1}H-NMR (300 MHz, $CDCl_3$) δ: 7.57-7.26 (*m*, 10H), 5.31 (*d,* 1 Vinyl-H, J = 2.8), 4.28 and 3.87 (*2d*, AB, 2H, J_{AB} = 12.5 Hz), 3.69 (*dd*, 1H, J_1 = 2.8 Hz, J_2 = 6.5 Hz), 1.76-1.64 (*m*, 1H), 3.69 (*dd*, 6H, J_1 = 1.4 Hz, J_2 = 6.7 Hz). ^{13}C-NMR (75 MHz, $CDCl_3$) δ: 152.5 (C), 136.8 (C), 129.9 (CH), 129.2 (C), 128.8 (CH), 128.4 (CH), 128.3 (CH), 127.5 (CH), 125.6 (CH), 93.7 (CH), 76.6 (CH), 64.0 (CH_2), 33.8 (CH), 18.7 (CH_3), 18.4 (CH_3). IR ($CHCl_3$): 3028*m*, 2956*s,* 2868*m*, 1947*w*, 1875*w*, 1806*w*, 1676*m*, 1604*w*, 1496*m*, 1454*m*, 1156*w*, 1074*m*,

1030*m*, 941*w*, 733*s,* 698*s*. Anal. Calcd. for $C_{19}H_{21}NO$ (279.38): C, 81.68; H, 7.58; N, 5.01. Found: C, 81.60; H, 7.65; N, 4.95.

2-Benzyl-3-*tert*-butyl-5-phenethyl-2,3-dihydro-isoxazole

N-benzyl-*N*-(1-*tert*-butyl-5-phenyl-pent-2-ynyl)-hydroxylamine (161 mg, 0.500 mmol), ZnI_2 (16 mg, 0.050 mmol, 10 mol%), and DMAP (6 mg, 0.05 mmol, 10 mol%) were stirred for 1 h at 23°C. Workup and purification using chromatography on silica gel (methylene chloride/hexane, 6:4) afforded 156 mg (97%) of the title compound as a colorless oil.

^{1}H-NMR (300 MHz, $CDCl_3$) δ: 7.45-7.20 (*m*, 10H), 4.51-4.50 (*m*, 1 Vinyl-H), 4.12 and 3.76 (*2d*, AB, 2H, J_{AB} = 12.9 Hz), 3.47-3.45 (*m*, 1H), 2.86 (*t*, 2H, J = 7.9 Hz), 2.54-2.48 (*m*, 2H), 0.78 (*s*, 9H). ^{13}C-NMR (75 MHz, $CDCl_3$) δ: 154.4 (C), 141.1 (C), 137.3 (C), 129.7 (CH), 128.4 (CH), 128.4 (CH), 128.2 (CH), 127.4 (CH), 126.1 (CH), 91.8 (CH), 79.5 (CH), 64.8 (CH_2), 35.1 (CH_2), 33.3 (C), 27.7 (CH_2), 25.5 (CH_3). IR ($CHCl_3$): 3028*m*, 2953*s,* 2864*s,* 1945*w*, 1869*w*, 1804*w*, 1677*s,* 1604*m*, 1496*s,* 1455*s,* 1361*s,* 1188*m*, 1074*m*, 1030*m*, 941*m*, 733*s*. Anal. Calcd. for $C_{22}H_{27}NO$ (321.46): C, 82.20; H, 8.47; N, 4.36. Found: C, 82.37; H, 8.48; N, 4.35.

2-Benzyl-3-*tert*-butyl-5-(*tert*-butyl-dimethyl-silanyloxymethyl)-2,3-dihydro-isoxazole

N-benzyl-*N*-[4-(*tert*-butyl-dimethyl-silanyloxy)-1-(dimethyl-ethyl)-but-2-ynyl]-hydroxylamine (181 mg, 0.500 mmol), ZnI_2 (16 mg, 0.050 mmol, 10 mol%), and DMAP (6 mg, 0.05 mmol, 10 mol%) were stirred for 28 h at 23°C. Workup and purification using chromatography on silica gel (methylene chloride/hexane, 6:4) afforded 168 mg (93%) of the title compound as a colorless oil.

^{1}H-NMR (300 MHz, $CDCl_3$) δ: 7.42-7.26 (*m*, 5H), 4.75-4.73 (*m*, 1 Vinyl-H), 4.20 (*s*, 2H), 4.13 and 3.76 (*2d*, AB, 2H, J_{AB} = 12.9 Hz), 3.49-3.47 (*m*, 1H), 0.91 (*s*, 9H), 0.79 (*s*, 9H), 0.08 (*d*, 6H, J = 1.6 Hz). ^{13}C-NMR (75 MHz, $CDCl_3$) δ: 154.4 (C), 137.2 (C), 129.7 (CH), 128.1 (CH), 127.3 (CH), 92.9 (CH), 79.3 (CH), 64.7 (CH_2), 57.3 (CH_2), 35.1 (C), 25.8 (CH_3), 25.5 (CH_3), 18.4 (C). IR ($CHCl_3$): 3032*w*, 2954*s,* 2859*s,* 1949*w*, 1882*w*, 1809*w*, 1686*m*, 1605*w*, 1462*m*, 1362*m*, 1455*m*, 1116*s,* 1006*w*, 938*m*, 838*s,* 776*s,* 730*m*, 697*m*, 606*w*. Anal. Calcd. for $C_{21}H_{35}SiNO_2$ (361.60): C, 69.75; H, 9.76; N, 3.87. Found: C, 69.63; H, 9.56; N, 4.03.

2-Benzyl-3-*tert*-butyl-5-phenyl-2,3-dihydro-isoxazole

N-benzyl-*N*-(1-*tert*-butyl-3-phenyl-prop-2-ynyl)-hydroxylamine (147 mg, 0.500 mmol), ZnI_2 (16 mg, 0.050 mmol, 10 mol%), and DMAP (6 mg, 0.05 mmol, 10 mol%) were stirred for 2 h at 23°C. Workup and purification using chromatography on silica gel (methylene chloride/hexane, 6:4) afforded 134 mg (91%) of the title compound as a white solid.

^{1}H-NMR (300 MHz, $CDCl_3$) δ: 7.54-7.26 (*m*, 10H), 5.25 (*d,* 1 Vinyl-H, J = 2.8), 4.24 and 3.83 (*2d*, AB, 2H, J_{AB} = 12.6 Hz), 3.65 (*d*, 1H, J = 3.1 Hz), 0.84 (*s,* 9H). ^{13}C-NMR (75 MHz, $CDCl_3$) δ: 152.3 (C), 137.0 (C), 129.9 (CH), 129.2 (C), 128.7 (CH), 128.3 (CH), 128.2 (CH), 127.4 (CH), 125.7 (CH), 92.4 (CH), 80.1 (CH), 64.8 (CH_2), 35.5 (C), 25.6 (CH_3). IR ($CHCl_3$): 3030*m*, 2953*s,* 2865*m*, 1949*w*, 1882*w*, 1807*w*, 1654*m*, 1601*w*, 1578*w*, 1494*m*, 1449*m*, 1362*m*, 1050*m*, 1024*m*, 898*w*, 764*s,* 720*s,* 697*s*. Anal. Calcd. for $C_{20}H_{23}NO$ (293.41):

C, 81.87; H, 7.90; N, 4.77. Found: C, 81.83; H, 7.85; N, 4.85.

2-Benzyl-5-phenethyl-3-phenyl-2,3-dihydro-isoxazole

N-benzyl-*N*-(1,5-diphenyl-pent-2-ynyl)-hydroxylamine (171 mg, 0.500 mmol), ZnI_2 (16 mg, 0.050 mmol, 10 mol%), and DMAP (6 mg, 0.05 mmol, 10 mol%) were stirred for 1 h at 23°C. Workup and purification using chromatography on silica gel (methylene chloride/hexane, 6:4) afforded 157 mg (92%) of the title compound as a colorless oil.

^{1}H-NMR (300 MHz, $CDCl_3$) δ: 7.42-7.13 (*m*, 15H), 4.86 (*s*, 1 Vinyl-H), 4.69-4.68 (*m*, 1H), 4.33 and 4.02 (*2d*, AB, 2H, J_{AB} = 12.8 Hz), 2.93 (*t*, 2H, J = 7.9 Hz), 2.61-2.55 (*m*, 2H). ^{13}C-NMR (75 MHz, $CDCl_3$) δ: 154.8 (C), 141.2 (C), 136.9 (C), 129.8 (CH), 128.6 (CH), 127.8 (CH), 127.6 (CH), 127.2 (CH), 126.4 (CH), 95.8 (CH), 73.2 (CH), 63.6 (CH_2), 33.1 (CH_2), 27.8 (CH_2). IR ($CHCl_3$): 3062*m*, 3028*s,* 2923*m*, 2860*m*, 1949*w*, 1879*w*, 1809*w*, 1752*w*, 1674*s,* 1603*m*, 1495*s,* 1454*s,* 1302*m*, 1220*m*, 1156*m*, 1075*m*, 1029*m*, 950*m*, 752*s,* 697*s*. Anal. Calcd. for $C_{24}H_{23}NO$ (341.45): C, 84.42; H, 6.79; N, 4.10. Found: C, 84.23; H, 6.90; N, 4.06.

2-Benzyl-5-(*tert*-butyl-dimethyl-silanyloxymethyl)-3-phenyl-2,3-dihydro-isoxazole

N-benzyl-*N*-[4-(*tert*-butyl-dimethyl-silanyloxy)-1-phenyl-but-2-ynyl]-hydroxylamine (191 mg, 0.500 mmol), ZnI_2 (16 mg, 0.050 mmol, 10 mol%), and DMAP (6 mg, 0.05 mmol, 10 mol%) were stirred for 32 h at 23°C. Workup and purification using chromatography on silica gel (methylene chloride/hexane, 6:4) afforded 157 mg (82%) of the title compound as a colorless oil.

^{1}H-NMR (300 MHz, $CDCl_3$) δ: 7.42-7.21 (*m*, 10H), 4.97-4.92 (*m*, 1 Vinyl-H), 4.35 and 4.06 (*2d*, AB, 2H, J_{AB} = 12.8 Hz), 4.31-4.29 (*m*, 1H), 0.92 (*s*, 9H), 0.11 (*s*, 6H). ^{13}C-NMR (75 MHz, $CDCl_3$) δ: 154.6 (C), 136.5 (C), 129.6 (CH), 128.5 (CH), 128.3 (CH), 127.5 (CH), 127.5 (CH), 127.1 (CH), 96.7 (CH), 73.0 (CH_2), 63.4 (CH), 57.4 (CH_2), 25.9 (CH_3), 18.4 (C), -5.1 (CH_3). IR ($CHCl_3$): 3030*m*, 2929*s,* 2857*s,* 1949*w*, 1880*w*, 1806*w*, 1681*m*, 1602*w*, 1455*m*, 1361*w*, 1255*m*, 1114*s,* 1006*m*, 939*m*, 838*s,* 777*s,* 697*s*. Anal. Calcd. for $C_{23}H_{31}SiNO_2$ (381.60): C, 72.40; H, 8.19; N, 3.67. Found: C, 72.48; H, 8.42; N, 3.71.

2-Benzyl-3,5-diphenyl-2,3-dihydro-isoxazole

N-benzyl-*N*-(1,3-diphenyl-prop-2-ynyl)-hydroxylamine (157 mg, 0.500 mmol), ZnI_2 (16 mg, 0.050 mmol, 10 mol%), and DMAP (6 mg, 0.05 mmol, 10 mol%) were stirred for 4 h at 23°C. Workup and purification using chromatography on silica gel (methylene chloride/hexane, 6:4) afforded 143 mg (91%) of the title compound as a white solid.

^{1}H-NMR (300 MHz, $CDCl_3$) δ: 7.60-7.23 (*m*, 15H), 5.44 (*d,* 1 Vinyl-H, J = 2.8), 5.07 (*d*, 1H, J = 2.8), 4.46 and 4.13 (*2d*, AB, 2H, J_{AB} = 12.8 Hz). ^{13}C-NMR (75 MHz, $CDCl_3$) δ: 153.2 (C), 142.4 (C), 136.7 (C), 129.9 (CH), 129.3 (CH), 129.0 (C), 128.8 (CH), 128.7 (CH), 128.6 (CH), 127.8 (CH), 127.4 (CH), 126.0 (CH), 95.9 (CH), 73.8 (CH), 63.6 (CH_2). IR ($CHCl_3$): 3062*m*, 3028*m*, 2888*w*, 1953*w*, 1884*w*, 1807*w*, 1651*m*, 1600*m*, 1494*s,* 1454*s,* 1320*m*, 1271*m*, 1220*m*, 1022*s,* 915*w*, 770*s,* 727*s,* 698*s*. Anal. Calcd. for $C_{22}H_{19}NO$ (313.40): C, 84.32; H, 6.11; N, 4.47. Found: C, 84.48; H, 6.29; N, 4.43. mp: 102-104°C.

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