SUPPORTING INFORMATION

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A Highly Stereoselective Addition of Lithiated Ynamides to Ellman–Davis Chiral *N*-*tert*-Butanesulfinyl Imines.

authored by

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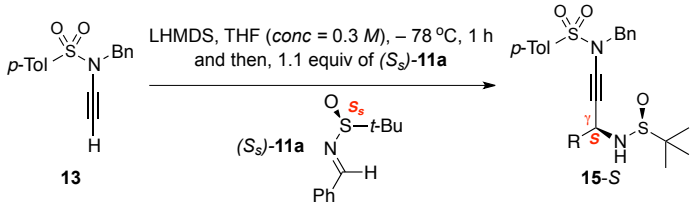
GENERAL EXPERIMENTAL INFORMATION

All reactions were performed in flame-dried glassware under nitrogen atmosphere. Solvents were distilled prior to use. Reagents were used as purchased from Aldrich, Acros, Alfa Aesar, or TCI unless otherwise noted. Chromatographic separations were performed using Silicycle 40-63μm SiO_2. ^1H NMR, ^{13}C NMR and ^{31}P NMR spectra were obtained on Varian VI-400 and VI-500 spectrometers using $CDCl_3$ with TMS or residual solvent as standard unless otherwise noted. Melting points were determined using a Laboratory Devices MEL-TEMP and are uncorrected/calibrated. Infrared spectra were obtained on Bruker EQUINOX 55 FTIR. TLC analysis was performed using Aldrich 254 nm polyester-backed plates (60 Å, 250 μm) and visualized using UV and $KMnO_4$ stains. Low-resolution mass spectra were obtained using an Agilent 1100 series LS/MSD and are APCI. All spectral data obtained for new compounds are reported here.

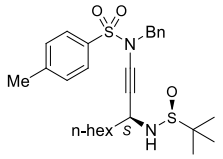
General Procedure for Additions of Lithiated Ynamides to Chiral Imines.



To a flamed-dried vial were added ynamide **13** (135.2 mg, 0.47 mmol) and THF (1.58 mL, ynamide *concn* = 0.30 *M*). To this solution was added LHMDS (0.71 mL, 1.0 *M* in THF) at -78 °C. After the mixture was stirred at -78 °C for 1.0 h, a solution of imine *(Ss)*-**11a**[1] (109.1 mg, 0.52 mmol) in THF (1 mL) was added over 1 min. The reaction mixture was then allowed to warm to -40 °C slowly and monitored using TLC analysis. When it was 9.0 h post addition of the imine, TLC analysis showed complete consumption of the starting material. The mixture was re-cooled to -78 °C, and H_2O (2 mL) was added to quench the reaction. The quenched mixture was extracted with equal volume of EtOAc, dried over Na_2SO_4, filtered, and concentrated under reduced pressure. The crude residue was purified using silica gel flash column chromatography [Gradient eluent: 8:1~1:1 Hexane/EtOAc + 3% NEt_3] to afford **15**-*S* (161.6 mg, 0.33 mmol) in 69% yield.

15-*S*: R_f = 0.18 [3:1 Hexane/EtOAc]; pale yellow solid; mp = 129–130 °C; ^1H NMR (400 MHz, $CDCl_3$) δ 1.16 (s, 9H), 2.41 (s, 3H), 3.51 (d, 1H, *J* = 5.6 Hz), 4.44 (d, 1H, *J* = 14.0 Hz), 4.51 (d, 1H, *J* = 14.0 Hz), 5.23 (d, 1H, *J* = 5.6 Hz), 7.24-7.29 (m, 12H), 7.72 (d, 2H, *J* = 8.4 Hz); ^{13}C NMR (100 MHz, $CDCl_3$) δ 21.6, 22.4, 50.6, 55.2, 56.2, 70.2, 79.9, 127.6, 127.7, 128.1, 128.2, 128.4, 128.5, 129.0, 129.7,

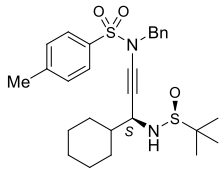
134.2, 134.4, 139.0, 144.5; IR (film) cm^{-1} 2249m, 1597m, 1494m, 1455m, 1363s, 1168s; HRMS (ESI): *m/z* calcd for $C_{27}H_{30}N_2O_3S_2$ $[M+H]^+$: 495.1771; found 495.1758.



16-*S*

Ynamide **16**-*S* (162.2 mg, 0.32 mmol) was prepared from the corresponding ynamide **13** (135.2 mg, 0.47 mmol) and imine **11b**[2] (113.3 mg, 0.52 mmol) in 68% yield.

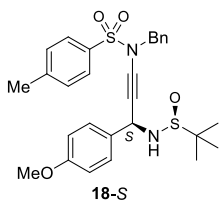
16-*S*: R_f = 0.52 [1:1 Hexane/EtOAc]; white solid; mp = 69–70 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 0.88 (t, 3H, *J* = 7.0 Hz), 1.16 (s, 9H), 1.18-1.29 (m, 8H), 1.48-1.64 (m, 2H), 2.43 (s, 3H), 3.13 (d, 1H, *J* = 5.6 Hz), 4.02-4.07 (m, 1H), 4.43 (d, 1H, *J* = 13.6 Hz), 4.50 (d, 1H, *J* = 13.6 Hz), 7.27-7.32 (m, 7H), 7.77 (d, 2H, *J* = 8.4 Hz); ^{13}C NMR (100 MHz, $CDCl_3$) δ 14.2, 21.7, 22.6, 22.7, 25.5, 28.9, 31.8, 37.0, 47.7, 55.5, 56.0, 71.2, 78.2, 127.9, 128.4, 128.6, 129.1, 129.8, 134.6, 134.7, 144.7; IR (film) cm^{-1} 2926brm, 2856m, 2252w, 1456m, 1364m, 1169s; mass spectrum (APCI): m/e (% relative intensity) 503 (100) $(M+H)^+$.



17-*S*

Ynamide **17**-*S* (183.3 mg, 0.36 mmol) was prepared from the corresponding ynamide **13** (135.2 mg, 0.47 mmol) and imine **11c**[3] (112.3 mg, 0.52 mmol) in 77% yield.

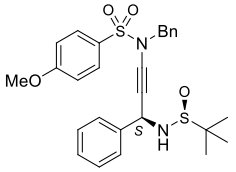
17-*S*: R_f = 0.51 [1:1 Hexane/EtOAc]; pale yellow solid; mp = 119–120 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 0.81-0.90 (m, 2H), 0.99-1.20 (m, 3H), 1.17 (s, 9H), 1.43-1.46 (m, 1H), 1.56-1.67 (m, 5H), 2.43 (s, 3H), 3.09 (d, 1H, *J* = 6.4 Hz), 3.88 (t, 1H, *J* = 6.0 Hz), 4.42 (d, 1H, *J* = 13.6 Hz), 4.50 (d, 1H, *J* = 14.0 Hz), 7.27-7.33 (m, 7H), 7.79 (d, 2H, *J* = 8.4 Hz); ^{13}C NMR (100 MHz, $CDCl_3$) δ 21.6, 22.6, 25.8, 25.9, 26.2, 27.8, 29.4, 43.3, 53.0, 55.4, 56.1, 70.1, 78.6, 127.9, 128.3, 128.5, 129.0, 129.8, 134.5, 134.6, 144.6; IR (film) cm^{-1} 2925brm, 2852w, 2250w, 1361m, 1168s, 1070m; mass spectrum (APCI): m/e (% relative intensity) 501 (90) $(M+H)^+$.



18-*S*

Ynamide **18**-*S* (129.9 mg, 0.25 mmol) was prepared from the corresponding ynamide **13** (111.7 mg, 0.39 mmol) and imine **11d**[3] (103.1 mg, 0.43 mmol) in 63% yield.

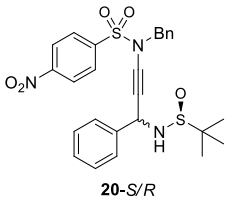
18-*S*: R_f = 0.28 [1:1 Hexane/EtOAc]; pale yellow oil; ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.14 (s, 9H), 2.41 (s, 3H), 3.48 (d, 1H, *J* = 5.2 Hz), 3.78 (s, 3H), 4.44 (d, 1H, *J* = 14.0 Hz), 4.50 (d, 1H, *J* = 13.6 Hz), 5.17 (d, 1H, *J* = 5.2 Hz), 6.80 (d, 2H, *J* = 8.8 Hz), 7.18-7.28 (m, 9H), 7.72 (d, 2H, *J* = 8.0 Hz); ^{13}C NMR (100 MHz, $CDCl_3$) δ 21.7, 22.6, 50.2, 55.36, 55.40, 56.2, 70.6, 79.8, 113.9, 127.9, 128.4, 128.6, 129.05, 129.14, 129.8, 131.3, 134.4, 134.6, 144.7, 159.5; IR (film) cm^{-1} 2248w, 1611w, 1456m, 1364m, 1250m, 1169s; mass spectrum (APCI): m/e (% relative intensity) 525 (100) $(M+H)^+$.



19-*S*

Ynamide **19**-*S* (228.9 mg, 0.45 mmol) was prepared from the corresponding ynamide (142.8 mg, 0.47 mmol) and imine **11a** (109.1 mg, 0.52 mmol) in 95% yield.

19-*S*: R_f = 0.28 [1:1 Hexane/EtOAc]; yellow oil; ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.15 (s, 9H), 3.53 (d, 1H, *J* = 5.6 Hz), 3.83 (s, 3H), 4.43 (d, 1H, *J* = 13.6 Hz), 4.51 (d, 1H, *J* = 14.0 Hz), 5.23 (d, 1H, *J* = 5.6 Hz), 6.89 (d, 2H, *J* = 8.8 Hz), 7.28 (d, 10H, *J* = 3.6 Hz), 7.75 (d, 2H, *J* = 8.8 Hz); ^{13}C NMR (100 MHz, $CDCl_3$) δ 22.6, 50.8, 55.3, 55.7, 56.3, 70.3, 80.3, 114.4, 114.9, 127.7, 128.2, 128.4, 128.55, 128.60, 129.1, 130.1, 134.4, 139.2, 163.7; IR (film) cm^{-1} 2248m, 1595m, 1497m, 1363m, 1262m, 1162s; mass spectrum (APCI): m/e (% relative intensity) 511 (100) $(M+H)^+$.

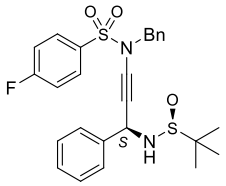


20-*S*/*R*

A separable 4:1 mixture of ynamides **20**-*S* (157.3 mg, 0.30 mmol) and **20**-*R* (39.3 mg, 0.07 mmol) were prepared from the corresponding ynamide (149.9 mg, 0.47 mmol) and imine **11a** (109.1 mg, 0.52 mmol) in 79% yield.

20-*S*: R_f = 0.62 [1:1 Hexane/EtOAc]; pale yellow oil; ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.20 (s, 9H), 3.52 (d, 1H, *J* = 6.8 Hz), 4.52 (d, 1H, *J* = 13.6 Hz), 4.61 (d, 1H, *J* = 14.0 Hz), 5.25 (d, 1H, *J* = 6.8 Hz), 7.26-7.42 (m, 12H), 7.99 (d, 2H, *J* = 8.8 Hz), 8.23 (d, 2H, *J* = 8.4 Hz). ^{13}C NMR (125 MHz, $CDCl_3$) δ 22.6, 51.3, 56.0, 56.6, 71.0, 79.4, 124.4, 127.5, 128.76, 128.81, 128.84, 129.1, 129.2, 129.3, 133.7, 138.9,

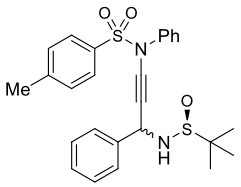
142.8, 150.5; IR (film) cm^{-1} 2251w, 1613m, 1531s, 1371m, 1348m, 1313m, 1172s; mass spectrum (APCI): m/e (% relative intensity) 526 (9) $(M + H)^+$.



21-*S*

Ynamide **21**-*S* (147.0 mg, 0.29 mmol) was prepared from the corresponding ynamide (135.0 mg, 0.47 mmol) and imine **11a** (109.1 mg, 0.52 mmol) in 62% yield.

21-*S*: R_f = 0.19 [4:1 Petroleum Ether/ EtOAc]; yellow solid; mp = 81-82 ^oC; ^1H NMR (600 MHz $CDCl_3$) 1.17 (s, 9H), 3.52 (d, 1H, *J*= 6.0 Hz), 4.46 (d, 1H, *J* = 12.0 Hz), 4.56 (d, 1H, *J* = 12.0 Hz), 5.24 (d, 1H, *J* = 6.0 Hz), 7.09 (t, 2H, *J* = 8.4 Hz), 7.26-7.29 (m, 10 H), 7.83 (dd, 2H, *J*= 5.4, 9.0 Hz); ^{13}C NMR (150 MHz, $CDCl_3$) 22.5, 51.0, 55.5, 56.3, 70.5, 79.9, 116.4 (d, $^2J_{F\text{-}C}$ = 22.7 Hz), 127.6, 128.2, 128.5, 128.58, 128.63, 129.1, 130.68 (d, $^3J_{F\text{-}C}$ = 9.6 Hz), 133.53 (d, $^4J_{F\text{-}C}$ = 2.7 Hz), 134.1, 139.0, 165.7 (d, $^1J_{F\text{-}C}$ = 254.7 Hz); IR (KBr) cm^{-1} 2246m, 1590m, 1491m, 1360m, 1239m, 1176s; mass spectrum (ESI): m/e (% relative intensity) 499 (100) $(M + H)^+$.

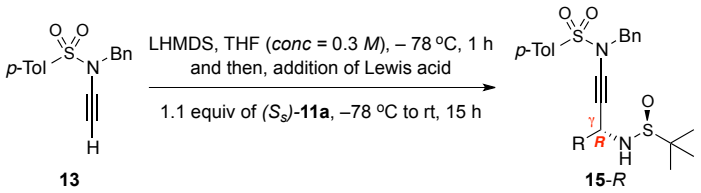


22-*S*/*R*

A separable 6:1 mixture of ynamides **22**-*S* (150.2 mg, 0.31 mmol) and **22**-*R* (25.0 mg, 0.05 mmol) were prepared from the corresponding ynamide (118.2 mg, 0.44 mmol) and imine **11a** (100.3 mg, 0.48 mmol) in 84% yield.

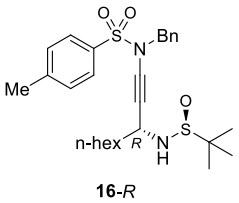
22-*S*: R_f = 0.46 [1:1 Hexane/EtOAc]; pale yellow oil; ^1H NMR (400 MHz, $CDCl_3$) δ 1.20 (s, 9H), 2.40 (s, 3H), 3.63 (d, 1H, *J* = 5.6 Hz), 5.35 (d, 1H, *J* = 5.6 Hz), 7.18 (d, 2H, *J* = 8.4 Hz), 7.26-7.41 (m, 8H), 7.48-7.52 (m, 4H). ^{13}C NMR (125 MHz, $CDCl_3$) δ 21.9, 22.7, 51.1, 56.5, 69.7, 80.6, 126.3, 128.0, 128.4, 128.45, 128.51, 128.8, 129.3, 129.7, 133.0, 138.7, 139.3, 145.1; IR (film) cm^{-1} 2254m, 1596m, 1492m, 1455m, 1373m, 1175s; mass spectrum (APCI): m/e (% relative intensity) 481 (64) $(M + H)^+$.

General Procedure for Additions with BF_3-OEt_2.



To a flamed-dried vial were charged with ynamide **13** (135.2 mg, 0.47 mmol) and THF (1.58 mL, ynamide *concn* = 0.3 *M*). To this solution at -78 °C was added LHMDS (0.71 mL, 1.0 *M* in THF). After the mixture was stirred at -78 °C for 1.0 h, a solution of imine *(Ss)*-**11a** (109.1 mg, 0.52 mmol) in THF (1 mL) pre-treated with BF_3-Et_2O (0.070 mL, 0.59 mmol) was added over 1 min. The resulting mixture was warmed to rt slowly, stirred overnight (~15 h), and monitored using TLC analysis. After complete consumption of the starting material, re-cooling of the mixture to -78 °C, H_2O (2 mL) was added to quench the reaction. The quenched mixture was extracted with equal volume of EtOAc, dried over Na_2SO_4, filtered, and concentrated under reduced pressure. The crude residue was purified using silica gel flash column chromatography [Gradient eluent: 8:1~1:1 Hex:EtOAc + 3% NEt_3] to afford **15**-*R* (234.4 mg, 0.47 mmol) in ≥95% yield.

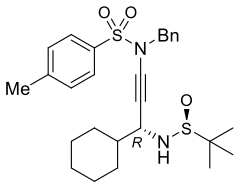
15-*R*: R_f = 0.30 [1:1 Hexane/EtOAc]; pale yellow oil; ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.13 (s, 9H), 2.43 (s, 3H), 3.32 (d, 1H, *J* = 4.0 Hz), 4.45 (d, 1H, *J* = 13.6 Hz), 4.55 (d, 1H, *J* = 14.0 Hz), 5.30 (d, 1H, *J* = 4.0 Hz), 7.24-7.31 (m, 12H), 7.70 (d, 2H, *J* = 8.4 Hz); ^{13}C NMR (100 MHz, $CDCl_3$) δ 21.8, 22.6, 51.5, 55.5, 56.0, 69.8, 80.2, 127.8, 128.0, 128.5, 128.6, 128.7, 128.9, 129.1, 129.9, 134.5, 134.7, 139.3, 144.8; IR (film) cm^{-1} 2250m, 1598m, 1455m, 1365s, 1169s; HRMS (ESI): *m/z* calcd for $C_{27}H_{30}N_2O_3S_2$ $[M+H]^+$: 495.1771; found 495.1751.



Ynamide **16**-*R* (186.7 mg, 0.37 mmol) were prepared from the corresponding ynamide (114.1 mg, 0.40 mmol) and imine **11b** (95.6 mg, 0.44 mmol) in 93% yield.

16-*R*: R_f = 0.25 [1:1 Hexane/EtOAc]; white solid; mp = 69–70 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 0.88 (t, 3H, *J* = 7.0 Hz), 1.13 (s, 9H), 1.21-1.29 (m, 8H), 1.50-1.67 (m, 2H), 2.43 (s, 3H), 3.12 (d, 1H, *J* = 5.2 Hz), 4.09-4.14 (m, 1H), 4.42 (d, 1H, *J* = 13.6 Hz), 4.52 (d, 1H, *J* = 14.0 Hz), 7.24-7.31 (m, 7H), 7.75 (d, 2H, *J* = 8.4 Hz); ^{13}C NMR (100 MHz, $CDCl_3$) δ 14.1, 21.7, 22.5, 22.6, 25.6, 28.8, 31.7, 37.5, 48.4, 55.5,

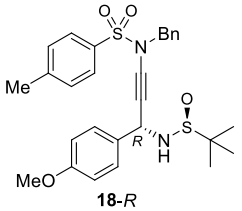
55.7, 70.6, 78.1, 127.8, 128.3, 128.5, 128.9, 129.7, 134.5, 134.7, 144.6; IR (film) cm^{-1} 2925m, 2857m, 2250w, 1597w, 1456m, 1364m, 1168s; mass spectrum (APCI): m/e (% relative intensity) 503 (100) $(M+H)^+$.



17-*R*

Ynamide **17**-*R* (213.6 mg, 0.43 mmol) were prepared from the corresponding ynamide (135.2 mg, 0.47 mmol) and imine **11c** (112.3 mg, 0.52 mmol) in 90% yield.

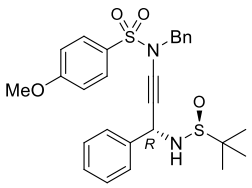
17-*R*: R_f = 0.20 [1:1 Hexane/EtOAc]; white solid; mp = 92–93 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 0.84-1.07 (m, 5H), 1.12 (s, 9H), 1.44-1.49 (m, 1H), 1.55-1.68 (m, 5H), 2.43 (s, 3H), 3.15 (d, 1H, J = 5.2 Hz), 3.99 (t, 1H, J = 5.0 Hz), 4.42 (d, 1H, J = 14.0 Hz), 4.54 (d, 1H, J = 14.0 Hz), 7.28-7.32 (m, 7H), 7.76 (d, 2H, J = 8.0 Hz); ^{13}C NMR (100 MHz, $CDCl_3$) δ 21.6, 22.5, 25.7, 25.9, 26.1, 27.5, 29.6, 43.8, 53.4, 55.4, 55.8, 69.2, 78.8, 127.8, 128.3, 128.5, 128.9, 129.7, 134.5, 134.6, 144.6; IR (film) cm^{-1} 2925m, 2852w, 2251w, 1452m, 1363m, 1168s; mass spectrum (APCI): m/e (% relative intensity) 501 (55) $(M+H)^+$.



18-*R*

Ynamide **18**-*R* (258.0 mg, 0.49 mmol) were prepared from the corresponding ynamide (135.2 mg, 0.47 mmol) and imine **11d** (124.8 mg, 0.52 mmol) in ≥95% yield.

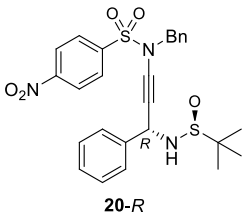
18-*R*: R_f = 0.15 [1:1 Hexane/EtOAc]; pale yellow oil; ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.09 (s, 9H), 2.38 (s, 3H), 3.34 (d, 1H, J = 3.6 Hz), 3.73 (s, 3H), 4.41 (d, 1H, J = 14.0 Hz), 4.51 (d, 1H, J = 14.0 Hz), 5.22 (d, 1H, J = 3.6 Hz), 6.77 (d, 2H, J = 8.4 Hz), 7.17-7.25 (m, 9H), 7.69 (d, 2H, J = 8.0 Hz); ^{13}C NMR (100 MHz, $CDCl_3$) δ 21.5, 22.37, 22.45, 50.7, 55.2, 55.3, 55.7, 69.8, 79.7, 113.9, 127.7, 128.2, 128.5, 128.77, 128.84, 129.7, 131.2, 134.3, 134.4, 144.6, 159.5; IR (film) cm^{-1} 2249w, 1611w, 1511m, 1364m, 1248m, 1169s; mass spectrum (APCI): m/e (% relative intensity) 525 (100) $(M+H)^+$.



19-*R*

Ynamide **19**-*R* (225.0 mg, 0.44 mmol) were prepared from the corresponding ynamide (142.8 mg, 0.47 mmol) and imine **11a** (109.1 mg, 0.52 mmol) in 93% yield.

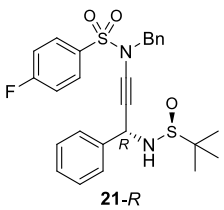
19-*R*: R_f = 0.18 [1:1 Hexane/EtOAc]; pale yellow solid; mp = 104–105 °C; ^{1}H NMR (500 MHz, $CDCl_3$) δ 1.12 (s, 9H), 3.40 (d, 1H, *J* = 3.5 Hz), 3.83 (s, 3H), 4.44 (d, 1H, *J* = 14.0 Hz), 4.54 (d, 1H, *J* = 14.0 Hz), 5.29 (d, 1H, *J* = 3.5 Hz), 6.90 (d, 2H, *J* = 9.0 Hz), 7.28 (d, 10H, *J* = 8.0 Hz), 7.74 (d, 2H, *J* = 9.0 Hz); ^{13}C NMR (125 MHz, $CDCl_3$) δ 22.5, 51.3, 55.3, 55.7, 55.8, 69.7, 80.3, 114.3, 127.6, 128.3, 128.4, 128.5, 128.7, 128.9, 129.0, 130.0, 134.4, 139.2, 163.7; IR (film) cm^{-1} 2251m, 1595m, 1497m, 1364m, 1262m, 1163s; mass spectrum (APCI): m/e (% relative intensity) 511 (90) $(M+H)^+$.



20-*R*

Ynamide **20**-*R* (62.3 mg, 0.12 mmol) were prepared from the corresponding ynamide (39.7 mg, 0.13 mmol) and imine **11a** (28.9 mg, 0.14 mmol) in 91% yield.

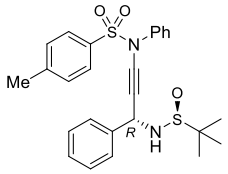
20-*R*: R_f = 0.31 [1:1 Hexane/EtOAc]; pale yellow oil; ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.16 (s, 9H), 3.45 (s, 1H), 4.55 (d, 1H, *J* = 14.0 Hz), 4.63 (d, 1H, *J* = 14.0 Hz), 5.33 (d, 1H, *J* = 3.6 Hz), 7.26-7.34 (m, 12H), 7.88 (d, 2H, *J* = 8.4 Hz), 8.19 (d, 2H, *J* = 8.4 Hz). ^{13}C NMR (100 MHz, $CDCl_3$) δ 22.6, 51.0, 56.1, 56.2, 70.4, 79.6, 124.3, 127.7, 128.8, 128.85, 128.88, 129.0, 129.08, 129.12, 133.8, 139.0, 143.0, 150.5; IR (film) cm^{-1} 2251m, 1531s, 1366m, 1349s, 1313m, 1174s; mass spectrum (APCI): m/e (% relative intensity) 526 (30) $(M + H)^+$.



21-*R*

Ynamide **21**-*R* (197.0 mg, 0.40 mmol) were prepared from the corresponding ynamide (135.0 mg, 0.47 mmol) and imine **11a** (109.1 mg, 0.52 mmol) in 84% yield.

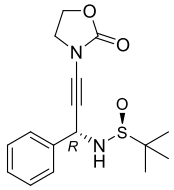
21-*R*: R_f = 0.16 [7:3 Petroleum Ether/ EtOAc]; mp = 84-85 ^{o}C; ^{1}H NMR (600 MHz $CDCl_3$) 1.14 (s, 9H), 3.37 (d, 1H, *J*= 3.6 Hz), 4.49 (d, 1H, *J* = 13.8 Hz), 4.58 (d, 1H, *J* = 13.8 Hz), 5.31 (d, 1H, *J* = 3.6 Hz), 7.09 (t, *J* = 8.4 Hz),7.27-7.34 (m, 10H,), 7.77-7.79 (m, 2H); ^{13}C NMR (150 MHz, $CDCl_3$) 22.5, 51.2, 55.6, 55.9, 69.9, 79.9, 116.3 (d, $^{2}J_{F\text{-}C}$ = 22.5 Hz), 127.6, 128.47, 128.53, 128.6, 128.8, 128.9, 130.6 (d, $^{3}J_{F\text{-}C}$ = 9.5 Hz), 133.6 (d, $^{4}J_{F\text{-}C}$ = 3.0 Hz), 134.1, 139.0, 165.6 (d, $^{1}J_{F\text{-}C}$ = 254.9 Hz); IR (KBr) cm^{-1} 2247w, 1590m, 1493m, 1366s, 1241m, 1178s; mass spectrum (ESI): m/e (% relative intensity) 521 (100) (M + Na)$^{+}$.



22-*R*

Ynamide **22**-*R* (114.3 mg, 0.24 mmol) were prepared from the corresponding ynamide (65.8 mg, 0.24 mmol) and imine **11a** (55.9 mg, 0.27 mmol) in 98% yield.

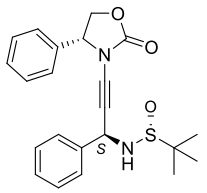
22-*R*: R_f = 0.24 [1:1 Hexane/EtOAc]; pale yellow solid; mp = 84–85 °C; ^{1}H NMR (500 MHz, $CDCl_3$) δ 1.18 (s, 9H), 2.40 (s, 3H), 3.48 (d, 1H, *J* = 4.0 Hz), 5.42 (d, 1H, *J* = 3.5 Hz), 7.19-7.40 (m, 11H), 7.50-7.51 (m, 4H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 21.8, 22.7, 51.5, 56.1, 68.9, 80.6, 126.2, 127.9, 128.35, 128.40, 128.7, 129.0, 129.2, 129.6, 133.0, 138.7, 139.4, 145.0; IR (film) cm^{-1} 2251m, 1595m, 1491m, 1455m, 1371s; mass spectrum (APCI): m/e (% relative intensity) 481 (88) (M+H)$^{+}$.



23-*R*

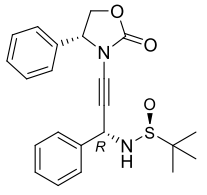
Ynamide **23**-*R* (145.2 mg, 0.45 mmol) were prepared from the corresponding ynamide (52.7 mg, 0.47 mmol) and imine **11a** (109.1 mg, 0.52 mmol) in 96% yield.

23-*R*: R_f = 0.22 [EtOAc]; pale yellow solid; mp = 131–132 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.21 (s, 9H), 3.69 (d, 1H, *J* = 4.0 Hz), 3.90-3.94 (m, 2H), 4.41 (t, 2H, *J* = 8.0 Hz), 5.43 (d, 1H, *J* = 4.0 Hz), 7.30-7.39 (m, 3H), 7.54 (d, 2H, *J* = 7.2 Hz)**;** ^{13}C NMR (100 MHz, $CDCl_3$) δ 22.6, 46.8, 51.2, 56.1, 63.2, 69.5, 76.8, 127.8, 128.6, 128.9, 139.0, 156.0**;** IR (film) cm^{-1} 2979brw, 2924w, 2264m, 1764s, 1477m, 1418m, 1201m**;** mass spectrum (APCI): m/e (% relative intensity) 321 (100) (M + H)$^{+}$.



24

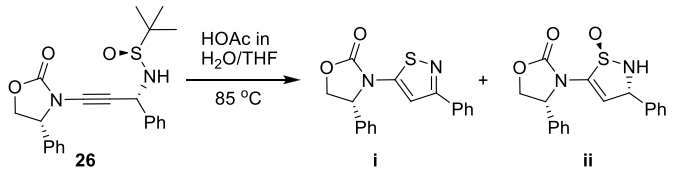
24: R_f = 0.26 [1:1 DCM/EtOAc]; white solid; mp = 150–151 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.09 (s, 9H), 3.48 (d, 1H, *J* = 4.4 Hz), 4.27 (dd, 1H, *J* = 7.2, 9.2 Hz), 4.74 (t, 1H, *J* = 9.0 Hz), 5.10 (dd, 1H, *J* = 7.2, 8.8 Hz), 5.29 (d, 1H, *J* = 4.4 Hz), 7.23-7.24 (m, 5H), 7.37-7.39 (m, 2H), 7.44-7.46 (m, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 22.4, 51.4, 55.9, 62.0, 70.8, 71.3, 75.7, 127.3, 127.7, 128.4, 128.7, 129.4, 129.6, 136.1, 138.6, 155.5; IR (film) cm-1 2267m, 1773s, 1457m, 1406m, 1182m; mass spectrum (APCI): m/e (% relative intensity) 397 (42) $(M + H)^+$.



26

26: R_f = 0.49 [1:1 DCM/EtOAc]; pale yellow oil; ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.10 (s, 9H), 3.40 (d, 1H, *J* = 4.4 Hz), 4.24 (dd, 1H, *J* = 7.2, 8.8 Hz), 4.72 (t, 1H, *J* = 8.8 Hz), 5.06 (t, 1H, *J* = 7.8 Hz), 5.27 (d, 1H, *J* = 4.0 Hz), 7.25-7.30 (m, 5H), 7.35-7.37 (m, 2H), 7.43-7.45 (m, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 22.4, 51.3, 55.9, 62.0, 70.8, 71.1, 75.6, 127.1, 127.6, 128.5, 128.8, 129.4, 129.6, 136.0, 139.0, 155.5; IR (film) cm^{-1} 2267m, 1773s, 1475m, 1457m, 1409m, 1181m; mass spectrum (APCI): m/e (% relative intensity) 397 (100) $(M + H)^+$.

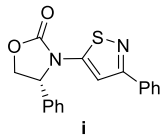
Acid Promoted 5-*endo-dig* Cyclization.



26 i ii

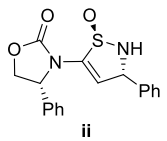
To a vial were added ynamide **26** (113.2 mg, 0.29 mmol), THF (0.50 mL), H_2O (0.050 mL), and HOAc (0.050 mL). The vial was sealed and heated to 85 °C. When the reaction was judged to be complete by TLC after 14.5 h, the mixture was cooled to rt and concentrated under reduced pressure. The crude residue was purified using silica gel flash column chromatography [Two isocratic eluent: (a) 4:1

Hexane/EtOAc and then (b) 1:1 Acetone/EtOAc] to afford **i** (23.0 mg, 0.07 mmol) in 25% yield and **ii** (29.7 mg, 0.09 mmol) in 31% yield.



i

i: R_f= 0.23 [3:1 hexanes/EtOAc]; white solid; mp = 207-208 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 4.38 (dd, 1H, *J* = 5.6, 8.8 Hz), 4.95 (t, 1H, *J* = 9.0 Hz), 5.36 (dd, 1H, *J* = 5.6, 9.2 Hz), 6.59 (s, 1H), 7.33-7.46 (m, 8H), 7.67-7.69 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 61.4, 71.8, 106.2, 126.4, 126.7, 128.8, 129.3, 129.9, 130.0, 134.8, 136.7, 155.3, 160.8, 164.7; IR (film) cm^{-1} 1745s, 1539m, 1389m, 1208m; mass spectrum (APCI): m/e (% relative intensity) 323 (100) $(M+H)^+$.



ii

ii: R_f= 0.11 [1:1 DCM/EtOAc]; white solid; mp = 198-199 °C. ^{1}H NMR (500 MHz, DMSO) δ 1.54 (s, 1H), 3.30 (dd, 1H, *J* = 3.5, 8.5 Hz), 3.95 (t, 1H, *J* = 9.0 Hz), 4.41 (dd, 1H, *J* = 3.5, 8.5 Hz), 4.51 (s, 1H), 4.63 (s, 1H), 5.95-5.97 (m, 2H), 6.25-6.45 (m, 8H); ^{13}C NMR (100 MHz, DMSO) δ 60.8, 67.0, 71.2, 117.5, 126.4, 127.3, 128.2, 128.6, 128.8, 129.3, 138.1, 138.6, 144.8, 154.0; IR (film) cm^{-1} 2959w, 2927w, 1768m, 1714s, 1645m, 1402m, 1187m; mass spectrum (APCI): m/e (% relative intensity) 341 (26) $(M+H)^+$.

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References

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