Supporting Information 1:

Regioselective Intramolecular Dipolar Cycloaddition of Azides and Unsymmetrical Alkynes

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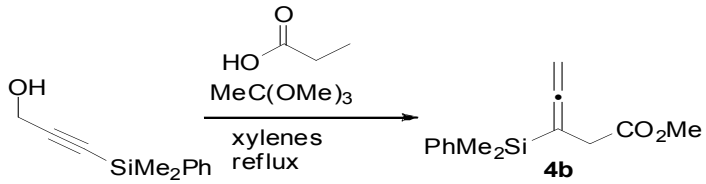
General Information:

All reactions were carried out in oven or flame dried glassware under an atmosphere of argon and using standard techniques for handling air sensitive materials. All solvents were reagent grade. Trimethylsilyltrifluoromethanesulfonate was freshly distilled before use. All other reagents were purchased from Aldrich of Alfa Aesar and used as supplied. All reactions were magnetically stirred and monitored by thin layer chromatography using Macherey-Nagel 0.20 mm silica gel 60 plates. Flash chromatography was performed with silica gel 60 (particle size 0.032-0.063mm) provided by Sorbent Technologies. Yields refer to chromatographically and spectroscopically pure compounds unless otherwise noted. ^{1}H NMR spectra were recorded using an internal deuterium lock at ambient temperature on a Varian 400MHz spectrometer. An internal reference of 7.24 was used for δ_H $CDCl_3$. Data are presented as follows: chemical shift (on a δ scale relative to $\delta_{TMS} = 0$), multiplicity (s = singlet, d = doublet, t = triplet, q = quartet, dd = doublet of doublets, m = multiplet, br = broad), coupling constant (*J*/Hz), and integration. Carbon-13 NMR spectra were recorded on a Varian 75 MHz spectrometer. An internal reference of δ_C 77.00 was used for $CDCl_3$. Infrared spectra were recorded on a Nexus 670 FT-IR spectrophotometer. Optical rotations were recorded on an Autopol III digital polarimeter at 589 nm and reported as follows: $[\alpha]_D^{20}$, concentration (*c* in g/100mL) and solvent. High resolution mass spectra were obtained on a Waters Q-TOF mass spectrometer in the Boston University Chemical Instrumentation Center. **CAUTION:** Sodium azide and low molecular weight organic compounds containing azide functionalities are an explosion risk. While we did not have any issues with the compounds described in this paper, it is important to take proper precautions when working with azides.

Experimental Procedures:

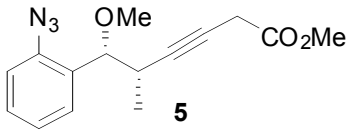


Methyl 3-(dimethyl(phenyl)silyl)penta-3,4-dienoate (4b): To a solution of 3-(dimethyl(phenyl)silyl)prop-2-yn-1-ol (5.0 g, 27.27 mmol)[1] in xylenes (50 mL) was

[1] For the synthesis of the know propargyl alcohol see: Kacprzynski, M. A.; May, T. L.; Kazane, S. A.; Hoyveda, A. H. *Angew. Chem. Int. Ed.* **2007**, *46*, 4554-4558.

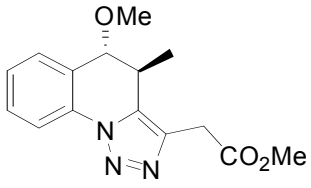
added trimethylorthoacetate (16.72 mL, 131.36 mmol) and propionic acid (0.098 mL, 1.31 mmol). The resulting solution was heated to reflux and stirred for 48 hours. After evaporation of solvents, the product was purified over silica gel (98:2 hexanes/ethyl acetate) to yield **4b** (3.13 g, 12.70 mmol, 47 % yield). ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.51 (m, 2H), 7.35 (m, 3H), 4.50 (t, J=2.8, 2H), 3.53 (s, 3H), 2.92 (t, J=2.8, 2H), 0.38 (s, 6H); ^{13}C NMR (75 MHz, $CDCl_3$): δ 211.1, 171.8, 137.1, 133.9, 129.3, 127.8, 87.6, 70.1, 51.6, 35.6, -3.1; IR (film) υ_{max} 3070, 2953, 1933, 1741, 1429, 1251, 1113 cm^{-1}; HRMS(CI, NH_3) m/z calc'd for $C_{14}H_{18}O_2Si$ $[M+H]^+$ 247.1154, found: 247.1198.

Two step procedure for triazole formation:



5

(5*S*, 6*R*)-methyl 6-(2-azidophenyl)-6-methoxy-5-methylhex-3-ynoate (5): A solution of allene **(R_a)-4a** (0.130 g, 0.5 mmol), 2-azidobenzaldehyde (0.088 g, 0.6 mmol) and methoxytrimethylsilane (0.063 g, 0.6 mmol) in propionitrile (3mL) was chilled to -78 ºC. Trimethylsilyltrifluoromethanesulfonate (0.116 mL, 0.6 mmol) was added slowly by microsyringe, and the solution was stirred for 12 hours at -78 ºC. The reaction was quenched with saturated aqueous sodium bicarbonate (5 mL) and warmed to room temperature. The product was extracted with ethyl acetate (3 X 5 mL), the organic layers were washed with water, dried with magnesium sulfate, filtered, and the solvents were removed under vacuum. Purification over silica gel (97:3 hexanes/ethyl acetate) yields **5** (0.102 g, 0.355 mmol, 71 % yield). ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.46 (m, 1H), 7.31 (m, 1H), 7.14 (m, 2H), 4.48 (d, J=6.0, 1H), 3.67 (s, 3H), 3.22 (s, 3H), 3.20 (d, J=2.4, 2H), 2.87 (m, 1H), 1.12 (d, J=7.2, 3H); ^{13}C NMR (75 MHz, $CDCl_3$): δ 169.0, 138.2, 131.0, 128.7, 128.4, 124.6, 117.7, 84.9, 80.0, 73.0, 57.3, 52.4, 32.4, 25.8, 16.3; IR (film) υ_{max} 3063, 2936, 2825, 2127, 1749, 1584, 1489, 1295, 1162 cm^{-1}; HRMS(CI, NH_3) m/z calc'd for $C_{15}H_{17}O_3N_3$ $[M+H]^+$ 288.1383, found: 288.1348; $[\alpha]_D^{20}$ +59.1 (c 5.5, CH_2Cl_2).



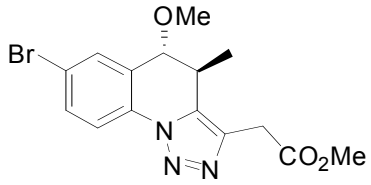
6a

Methyl 2-((4*S*, 5*R*)-5-methoxy-4-methyl-4,5-dihydro-[1,2,3]trazolo[1,5-*a*]quinolin-3-yl)acetate (6a): A solution of **5** (0.011 g, 0.038 mmol) in toluene (1 mL) in a sealed tube was heated to 110 ºC and stirred 5 hours. The reaction was cooled to room temperature, and the solvents are removed under vacuum. Purification over silica gel (gradient elution, 95:5 to 80:20 DCM/ethyl acetate) yields **6a** (0.010 g, 0.035 mmol, 90 % yield). ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.16 (m, 1H), 7.53 (m, 1H), 7.42 (m, 1H), 7.36 (m, 2H), 4.18 (d, J=2.4, 1H), 3.84 (dd, J=16.4, 36.0, 2H), 3.62 (s, 3H), 3.60 (m, 1H), 3.17 (s, 3H), 1.07 (d, J=7.6, 3H); ^{13}C NMR (75 MHz, $CDCl_3$): δ 170.5, 137.3, 133.5, 133.0, 131.0, 127.1, 123.7, 117.4, 80.1, 56.0, 52.3, 31.4, 31.3, 16.3; IR (film) υ_{max} 2952, 2824, 1741, 1618, 1594,

1494, 1235, 1146 cm^{-1}; HRMS(CI, NH_3) m/z calc'd for $C_{15}H_{17}O_3N_3$ $[M+H]^+$ 288.1383, found: 288.1348; $[\alpha]_D^{20}$ +181.9 (c 8.0, CH_2Cl_2).

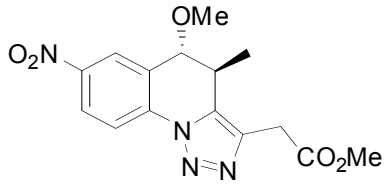
One step procedure for triazole formation:

Methyl 2-((4*S*, 5*R*)-5-methoxy-4-methyl-4,5-dihydro-[1,2,3]trazolo[1,5-*a*]quinolin-3-yl)acetate (6a): A solution of allene **(R_a)-4a** (0.130 g, 0.5 mmol), 2-azidobenzaldehyde (0.088 g, 0.6 mmol) and methoxytrimethylsilane (0.063 g, 0.6 mmol) in propionitrile (3 mL) was chilled to -78 ºC. Trimethylsilyltrifluoromethanesulfonate (0.116 mL, 0.6 mmol) was added slowly by microsyringe, and the solution was stirred for 12 hours at -78 ºC. The reaction was quenched with saturated aqueous sodium bicarbonate (5 mL) and warmed to room temperature. The product was extracted with ethyl acetate (3 X 5 mL), the organic layers were washed with water, dried with magnesium sulfate, filtered, and the solvents were removed under vacuum. The crude reaction mixture was dissolved in toluene (3 mL) in a sealed tube, heated to 70 ºC and stirred 12 hours. The reaction was cooled to room temperature, and the solvents were removed under vacuum. Purification over silica gel (gradient elution, 95:5 to 80:20 DCM/ethyl acetate) yields **6a** (0.110 g, 0.383 mmol, 77 % yield). This product was spectroscopically identical to the product obtained in the two step procedure.



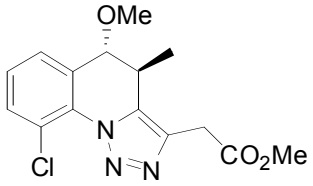
6b

Methyl 2-((4*S*, 5*R*)-7-bromo-5-methoxy-4-methyl-4,5-dihydro-[1,2,3]trazolo[1,5-*a*]quinolin-3-yl)acetate (6b): The same procedure as the one step procedure for **6a** using 2-azido-5-bromobenzaldehyde (0.136 g, 0.6 mmol) yields **6b** (0.109 g, 0.298 mmol, 60 % yield). ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.05 (d, J=8.8, 1H), 7.67 (m, 1H), 7.57 (m, 1H), 4.13 (d, J=2.8, 1H), 3.83 (dd, J=16.8, 49.6, 2H), 3.71 (s, 3H), 3.60 (m, 1H), 3.21 (s, 3H), 1.08 (d, J=7.6, 3H); ^{13}C NMR (75 MHz, $CDCl_3$): δ 170.3, 137.5, 133.6, 133.4, 133.4, 132.0, 125.9, 120.4, 119.0, 79.9, 56.2, 52.3, 31.3, 16.1; IR (film) υ_{max} 2951, 2824, 1742, 1492, 1237, 1193 cm^{-1}; HRMS(CI, NH_3) m/z calc'd for $C_{15}H_{16}O_3N_3Br$ $[M+Na]^+$ 388.0273, found: 388.0291; $[\alpha]_D^{20}$ +45.8 (c 3.6, CH_2Cl_2).



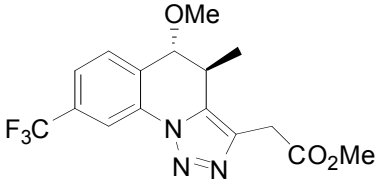
6c

Methyl 2-((4*S*, 5*R*)-5-methoxy-4-methyl-7-nitro-4,5-dihydro-[1,2,3]trazolo[1,5-*a*]quinolin-3-yl)acetate (6c): The same procedure as the one step procedure for **6a** using 2-azido-5-nitrobenzaldehyde (0.115 g, 0.6 mmol) yields **6c** (0.109 g, 0.328 mmol, 66 % yield). ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.45 (m, 1H), 8.35 (m, 2H), 4.29 (d, J=2.8, 1H), 3.86 (dd, J=16.4, 29.2, 2H), 3.73 (s, 3H), 3.69 (m, 1H), 3.26 (s, 3H), 1.12 (d, J=7.2, 3H); ^{13}C NMR (75 MHz, $CDCl_3$): δ 170.0, 145.9, 138.0, 137.1, 134.1, 126.1, 126.0, 125.2, 118.1, 79.6, 56.4, 52.3, 31.1, 16.1; IR (film) υ_{max} 2953, 2827, 1741, 1530, 1497, 1346, 1253, 1140 cm^{-1}; HRMS(CI, NH_3) m/z calc'd for $C_{15}H_{16}O_5N_4$ $[M+H]^+$ 333.1199, found: 333.1213; $[\alpha]_D^{20}$ +91.6 (c 1.6, CH_2Cl_2).



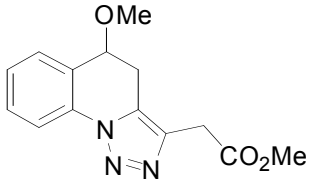
6d

Methyl 2-((4*S*, 5*R*)-9-chloro-5-methoxy-4-methyl-4,5-dihydro-[1,2,3]trazolo[1,5-*a*]quinolin-3-yl)acetate (6d): The same procedure as the one step procedure for **6a** using 2-azido-3-chlorobenzaldehyde (0.109 g, 0.6 mmol) yields **6d** (0.105 g, 0.326 mmol, 65 % yield). ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.61 (d, J=8.0, 1H), 7.31 (m, 2H), 4.15 (d, J=2.0, 1H), 3.85 (dd, J=16.4, 63.2, 2H), 3.70 (s, 3H), 3.55 (m, 1H), 3.16 (s, 3H), 1.07 (d, J=7.2, 3H); ^{13}C NMR (75 MHz, $CDCl_3$): δ 170.3, 136.3, 134.8, 133.5, 130.6, 129.6, 127.6, 127.4, 125.0, 80.7, 56.0, 52.2, 31.2, 15.4; IR (film) υ_{max} 2976, 2949, 1743, 1481, 1250, 1193 cm^{-1}; HRMS(CI, NH_3) m/z calc'd for $C_{15}H_{16}O_3N_3Cl$ $[M+H]^+$ 322.0958, found: 322.0965; $[\alpha]_D^{20}$ +267.3 (c 1.1, CH_2Cl_2).



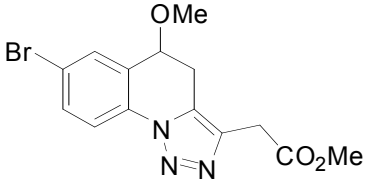
6e

Methyl 2-((4*S*, 5*R*)-5-methoxy-4-methyl-8-(trifluoromethyl)-4,5-dihydro-[1,2,3]trazolo[1,5-*a*]quinolin-3-yl)acetate (6e): The same procedure as the one step procedure for **6a** using 2-azido-4-(trifluoromethyl)benzaldehyde (0.129 g, 0.6 mmol) yields **6e** (0.107 g, 0.301 mmol, 60 % yield). ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.46 (s, 1H), 7.60 (m, 2H), 4.23 (d, J=2.8, 1H), 3.85 (dd, J=16.4, 32.8, 2H), 3.71 (s, 3H), 3.65 (m, 1H), 3.21 (s, 3H), 1.09 (d, J=7.6, 3H); ^{13}C NMR (75 MHz, $CDCl_3$): δ 170.2, 137.7, 133.6, 133.2, 131.4, 127.4, 123.7, 114.6, 79.7, 56.2, 52.2, 31.2, 16.1; IR (film) υ_{max} 2954, 2827, 1744, 1488, 1317, 1249, 1152 cm^{-1}; HRMS(CI, NH_3) m/z calc'd for $C_{16}H_{16}O_3N_3F_3$ $[M+Na]^+$ 378.1041, found: 378.1038; $[\alpha]_D^{20}$ +166.8 (c 1.9, CH_2Cl_2).



6f

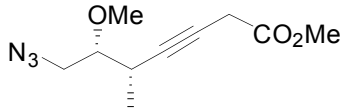
Methyl 2-(5-methoxy-4,5-dihydro-[1,2,3]trazolo[1,5-*a*]quinolin-3-yl)acetate (6f): The same procedure as the one step procedure for **6a** using achiral allene **4b** (0.123 g, 0.5 mmol) yields **6f** (0.057 g, 0.209 mmol, 42 % yield). ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.17 (d, J=8.0, 1H), 7.52 (m, 2H), 7.34 (m, 1H), 4.49 (t, J=4.4, 1H), 3.85 (dd, J=16.8, 31.2, 2H), 3.71 (s, 3H), 3.34 (m, 1H), 3.27 (s, 3H), 3.12 (m, 1H); ^{13}C NMR (75 MHz, $CDCl_3$): δ 170.5, 137.6, 133.3, 130.2, 129.3, 128.7, 127.2, 125.3, 117.3, 73.6, 56.1, 52.2, 31.3, 25.7; IR (film) υ_{max} 2951, 2827, 1740, 1559, 1495, 1384, 1232, 1197 cm^{-1}; HRMS(CI, NH_3) m/z calc'd for $C_{14}H_{15}O_3N_3$ $[M+Na]^+$ 296.1011, found: 296.1017.



6g

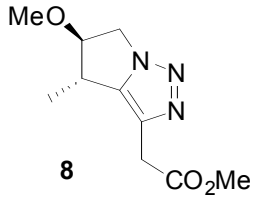
Methyl 2-(7-bromo-5-methoxy-4,5-dihydro-[1,2,3]trazolo[1,5-*a*]quinolin-3-yl)acetate (6g): The same procedure **6f** using 2-azido-5-bromobenzaldehyde (0.136 g, 0.6 mmol) yields **6g** (0.087 g, 0.247 mmol, 49 % yield). ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.04 (m, 1H), 7.64 (m, 2H), 4.46 (t, J=5.2, 1H), 3.85 (dd, J=16.8, 23.2, 2H), 3.71

(s, 3H), 3.32 (s, 3H), 3.19 (m, 2H); ^{13}C NMR (75 MHz, $CDCl_3$): δ 170.3, 137.8, 133.0, 131.8, 128.6, 127.6, 120.7, 118.9, 73.2, 56.4, 52.3, 31.2, 25.5; IR (film) υ_{max} 2951, 2827, 1740, 1490, 1437, 1194 cm^{-1}; HRMS(CI, NH_3) m/z calc'd for $C_{14}H_{14}O_3N_3Br$ $[M+H]^+$ 352.0297, found: 352.0311.



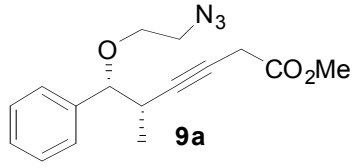
7

(5*S*, 6*R*)-methyl 7-azido-6-methoxy-5-methylhept-3-ynoate (7): A solution of allene **(*R*$_a$)-4a** (0.130 g, 0.5 mmol) and azidoacetaldehyde dimethyl acetal (0.131 g, 1.0 mmol) in propionitrile (3mL) was chilled to -78 ºC. Trimethylsilyltrifluoromethanesulfonate (0.116 mL, 0.6 mmol) was added slowly by microsyringe, and the solution was stirred for 12 hours at -78 ºC. The reaction was quenched with saturated aqueous sodium bicarbonate (5 mL) and warmed to room temperature. The product was extracted with ethyl acetate (3 X 5 mL), the organic layers were washed with water, dried with magnesium sulfate, filtered, and the solvents were removed under vacuum. Purification over silica gel (97:3 hexanes/ethyl acetate) yields **7** (0.044 g, 0.195 mmol, 39 % yield). ^{1}H NMR (400 MHz, $CDCl_3$): δ 3.71 (s, 3H), 3.48 (m, 2H), 3.47 (s, 3H), 3.45 (m, 1H), 3.24 (d, J=2.4, 2H), 3.18 (m, 1H), 1.21 (d, J=6.8, 3H); ^{13}C NMR (75 MHz, $CDCl_3$): δ 169.0, 84.2, 83.9, 74.1, 58.6, 52.5, 51.9, 28.8, 25.7, 17.2; IR (film) υ_{max} 2979, 2938, 2832, 2100, 1747, 1438, 1345, 1269, 1198 cm^{-1}; HRMS(CI, NH_3) m/z calc'd for $C_{10}H_{15}O_3N_3$ $[M+H]^+$ 226.1192, found: 226.1197; $[\alpha]_D^{20}$ -30.0 (c 15.0, CH_2Cl_2).



8

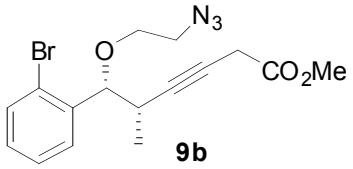
Methyl 2-((4*S*, 5*R*)-5-methoxy-4-methyl-5,6-dihydro-4*H*-pyrrolo[1,2-*c*][1,2,3]trazol-3-yl)acetate (5): A solution of **7** (0.011 g, 0.049 mmol) in toluene (1 mL) in a sealed tube was heated to 110 ºC and stirred 5 hours. The reaction was cooled to room temperature, and the solvents were removed under vacuum. Purification over silica gel (gradient elution, 95:5 to 80:20 DCM/ethyl acetate) yields **8** (0.010 g, 0.044 mmol, 90 % yield). ^{1}H NMR (400 MHz, $CDCl_3$): δ 4.58 (q, J=5.6, 1H), 4.22 (m, 1H), 3.76 (dd, J=17.2, 17.6), 3.70 (s, 3H), 3.34 (s, 3H), 3.30 (m, 1H), 1.35 (d, J=7.2, 3H); ^{13}C NMR (75 MHz, $CDCl_3$): δ 170.6, 141.6, 133.4, 90.7, 57.6, 52.2, 51.6, 36.8, 31.5, 16.7; IR (film) υ_{max} 2979, 2938, 2832, 1747, 1438, 1345, 1269, 1198 cm^{-1}; HRMS(CI, NH_3) m/z calc'd for $C_{10}H_{15}O_3N_3$ $[M+H]^+$ 226.1192, found: 226.1188; $[\alpha]_D^{20}$ +4.9 (c 12.1, CH_2Cl_2).



9a

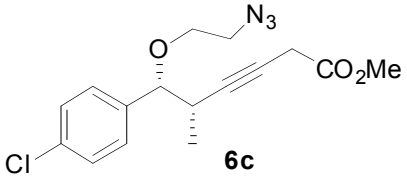
(5*S*, 6*R*)-methyl 6-(2-azidoethoxy)-5-methyl-6-phenylhex-3-ynoate (9a): A solution of allene **(*R*$_a$)-4** (0.130 g, 0.5 mmol), benzaldehyde (0.064 g, 0.6 mmol) and (2-azidoethoxy)(*tert*-butyl)dimethylsilane (0.121 g, 0.6 mmol) in propionitrile (3mL) was chilled to -78 ºC. Trimethylsilyltrifluoromethanesulfonate (0.116 mL, 0.6 mmol) was added slowly by microsyringe, and the solution was stirred for 12 hours at -78 ºC. The

reaction was quenched with saturated aqueous sodium bicarbonate (5 mL) and warmed to room temperature. The product was extracted with ethyl acetate (3 X 5 mL), the organic layers were washed with water, dried with magnesium sulfate, filtered, and the solvents were removed under vacuum. Purification over silica gel (97:3 hexanes/ethyl acetate) yields **9a** (0.109 g, 0.362 mmol, 72 % yield). ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.30 (m, 5H), 4.18 (d, J=6.8, 1H), 3.67 (s, 3H), 3.50 (m, 2H), 3.33 (m, 2H), 3.15 (d, J=2.0, 2H), 2.80 (m, 1H), 1.22 (d, J=6.8, 3H); ^{13}C NMR (75 MHz, $CDCl_3$): δ 169.0, 139.5, 128.0, 127.8, 127.4, 85.4, 84.8, 73.6, 68.1, 52.3, 50.9, 33.7, 25.7, 16.9; IR (film) υ_{max} 3030, 2933, 2871, 2102, 1744, 1436, 1267, 1197, 1111 cm^{-1}; HRMS(CI, NH_3) m/z calc'd for $C_{16}H_{19}O_3N_3$ $[M+Na]^+$ 324.1324, found: 324.1319; $[\alpha]_D^{20}$ +10.7 (c 1.4, CH_2Cl_2).



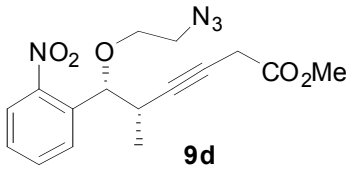
9b

(5*S*, 6*R*)-methyl 6-(2-azidoethoxy)-6-(2-bromophenyl)-5-methylhex-3-ynoate (9b): Same procedure as **9a** using 2-bromobenzaldehyde (0.111 g, 0.6 mmol) yields **9b** (0.170 g, 0.447 mmol, 89 % yield). ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.52 (m, 2H), 7.34 (m, 1H), 7.14 (m, 1H), 4.79 (d, J=6.0, 1H), 3.68 (s, 3H), 3.53 (m, 2H), 3.37 (m, 1H), 3.36 (m, 1H), 3.19 (d, J=2.4, 2H), 2.89 (m, 1H), 1.20 (d, J=6.8, 3H); ^{13}C NMR (75 MHz, $CDCl_3$): δ 168.9, 138.8, 132.5, 129.2, 128.7, 127.5, 123.9, 84.5, 82.8, 73.2, 68.5, 52.3, 50.8, 32.3, 25.8, 15.9; IR (film) υ_{max} 2934, 2832, 2104, 1749, 1436, 1266, 1110 cm^{-1}; HRMS(CI, NH_3) m/z calc'd for $C_{16}H_{18}O_3N_3Br$ $[M+Na]^+$ 402.0429, found: 402.0421; $[\alpha]_D^{20}$ +32.6 (c 1.5, CH_2Cl_2).



6c

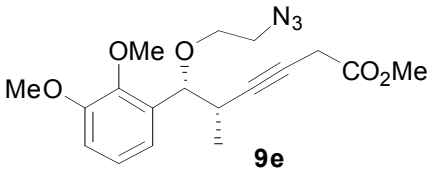
(5*S*, 6*R*)-methyl 6-(2-azidoethoxy)-6-(4-chlorophenyl)-5-methylhex-3-ynoate (6c): Same procedure as **6a** using 4-chlorobenzaldehyde (0.084 g, 0.6 mmol) yields **6c** (0.127 g, 0.378 mmol, 76 % yield). ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.27 (m, 4H), 4.13 (d, J=7.2, 1H), 3.68 (s, 3H), 3.47 (m, 2H), 3.32 (m, 2H), 3.14 (d, J=2.4, 2H), 2.76 (m, 1H), 1.22 (d, J=7.2, 3H); ^{13}C NMR (75 MHz, $CDCl_3$): δ 168.9, 138.1, 133.6, 128.8, 128.2, 84.9, 84.4, 74.1, 68.2, 52.3, 50.8, 33.7, 25.7, 17.1; IR (film) υ_{max} 2933, 2872, 2105, 1748, 1491, 1436, 1268, 1189 cm^{-1}; HRMS(CI, NH_3) m/z calc'd for $C_{16}H_{18}O_3N_3Cl$ $[M+Na]^+$ 358.0934, found: 358.0946; $[\alpha]_D^{20}$ +1.8 (c 1.6, CH_2Cl_2).



9d

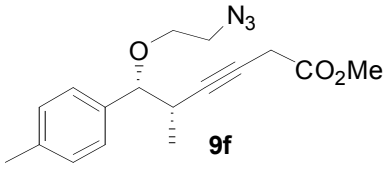
(5*S*, 6*R*)-methyl 6-(2-azidoethoxy)-5-methyl-6-(2-nitrophenyl)hex-3-ynoate (9d): Same procedure as **9a** using 2-nitrobenzaldehyde (0.091 g, 0.6 mmol) yields **9d** (0.150 g, 0.433 mmol, 87 % yield). ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.82 (m, 2H), 7.63 (m, 1H), 7.43 (m, 1H), 5.06 (d, J=7.6, 1H), 3.66 (s, 3H), 3.59 (m, 2H), 3.40 (m, 2H), 3.11 (d, J=2.4, 2H), 2.74 (m, 1H), 1.27 (d, J=6.8, 3H); ^{13}C NMR (75 MHz, $CDCl_3$): δ 168.7, 149.8, 135.4, 133.0, 128.5, 123.9, 83.4, 79.5, 74.1, 68.9, 52.3, 50.7, 34.0, 25.6, 17.0; IR (film) υ_{max} 2937, 2875, 2106, 1748, 1528, 1437,

1355, 1270, 1196 cm^{-1}; HRMS(CI, NH_3) m/z calc'd for $C_{16}H_{18}O_5N_4$ $[M+Na]^+$ 369.1175, found: 369.1161; $[\alpha]_D^{20}$ +214.7 (c 4.0, CH_2Cl_2).



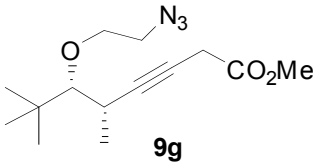
9e

(5*S*, 6*R*)-methyl 6-(2-azidoethoxy)-6-(2,3-dimethoxyphenyl)-5-methylhex-3-ynoate (9e): Same procedure as **9a** using 2,3-dimethoxybenzaldehyde (0.100 g, 0.6 mmol) yields **9e** (0.133 g, 0.368 mmol, 74 % yield). ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.05 (m, 2H), 6.84 (m, 1H), 4.71 (d, J=6.8, 1H), 3.85(s, 3H), 3.83(s, 3H), 3.65 (s, 3H), 3.51 (m, 2H), 3.32 (m, 2H), 3.16 (d, J=2.4, 2H), 2.92 (m, 1H), 1.21 (d, J=6.8, 3H); ^{13}C NMR (75 MHz, $CDCl_3$): δ 169.0, 152.1, 147.2, 133.2, 123.8, 119.5, 111.5, 85.3, 78.3, 72.9, 68.1, 60.7, 55.6, 52.3, 50.8, 32.3, 25.8, 16.6; IR (film) υ_{max} 2936, 2875, 2104, 1749, 1479, 1355, 1265 cm^{-1}; HRMS(CI, NH_3) m/z calc'd for $C_{18}H_{23}O_5N_3$ $[M+Na]^+$ 384.1535, found: 384.1526; $[\alpha]_D^{20}$ +30.4 (c 1.2, CH_2Cl_2).



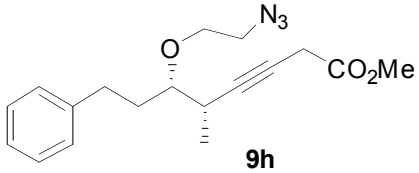
9f

(5*S*, 6*R*)-methyl 6-(2-azidoethoxy)-5-methyl-6-*p*-tolylhex-3-ynoate (9f): Same procedure as **9a** using *p*-tolualdehyde (0.072 g, 0.6 mmol) yields **9f** (0.119 g, 0.377 mmol, 76 % yield). ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.22 (d, J=8.0, 2H), 7.13 (d, J=7.6, 2H), 4.14 (d, J=7.2, 1H), 3.68 (s, 3H), 3.50 (m, 2H), 3.31 (m, 2H), 3.16 (d, J=2.4, 2H), 2.79 (m, 1H), 2.33 (s, 3H), 1.21 (d, J=6.8, 3H); ^{13}C NMR (75 MHz, $CDCl_3$): δ 169.0, 137.4, 136.4, 128.6, 127.4, 127.3, 85.2, 84.9, 73.5, 67.9, 52.2, 50.8, 33.6, 29.6, 25.7, 21.1, 17.0; IR (film) υ_{max} 2919, 2850, 2103, 1750, 1456, 1437, 1340, 1266, 1173 cm^{-1}; HRMS(CI, NH_3) m/z calc'd for $C_{17}H_{21}O_3N_3$ $[M+Na]^+$ 338.1481, found: 338.1475; $[\alpha]_D^{20}$ +4.0 (c 1.5, CH_2Cl_2).



9g

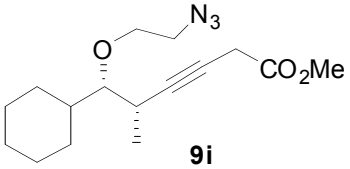
(5*S*, 6*R*)-methyl 6-(2-azidoethoxy)-5,7,7-trimethyloct-3-ynoate (9g): Same procedure as **9a** using trimethylacetaldehyde (0.052 g, 0.6 mmol) yields **9g** (0.085 g, 0.302 mmol, 60 % yield). ^{1}H NMR (400 MHz, $CDCl_3$): δ 4.01 (m, 1H), 3.70 (s, 3H), 3.66 (m, 1H), 3.34 (m, 2H), 3.23 (d, J=2.4, 2H), 3.10 (d, J=4.0, 1H), 2.73 (m, 1H), 1.22 (d, J=6.8, 3H), 0.94(s, 9H); ^{13}C NMR (75 MHz, $CDCl_3$): δ 169.2, 90.3, 88.9, 72.1, 52.4, 51.4, 36.5, 26.8, 25.8, 16.6; IR (film) υ_{max} 2955, 2105, 1750, 1437, 1341, 1266, 1172 cm^{-1}; HRMS(CI, NH_3) m/z calc'd for $C_{14}H_{23}O_3N_3$ $[M+H]^+$ 282.1818, found: 282.1827; $[\alpha]_D^{20}$ +24.5 (c 2.0, CH_2Cl_2).



9h

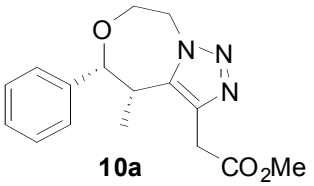
(5*S*, 6*S*)-methyl 6-(2-azidoethoxy)-5-methyl-8-phenyloct-3-ynoate (9h): Same procedure as **9a** using hydrocinnamaldehyde (0.081 g, 0.6 mmol) yields **9h** (0.060 g, 0.184 mmol, 37 % yield). ^{1}H NMR (400

MHz, $CDCl_3$): δ 7.25 (m, 2H), 7.19 (m, 3H), 3.74 (m, 1H), 3.68 (s, 3H), 3.63 (m, 1H), 3.38 (m, 2H), 3.25 (d, J=2.4, 2H), 2.81 (m, 1H), 2.67 (m, 2H), 1.92 (m, 2H), 1.18 (d, J=7.2, 3H); ^{13}C NMR (75 MHz, $CDCl_3$): δ 169.1, 142.2, 128.4, 128.3, 125.8, 125.7, 85.4, 82.5, 73.2, 68.9, 52.4, 51.2, 33.6, 31.4, 30.3, 30.1, 25.9, 16.8; IR (film) υ_{max} 3026, 2951, 2104, 1749, 1455, 1342, 1265, 1170 cm^{-1}; HRMS(CI, NH_3) m/z calc'd for $C_{18}H_{23}O_3N_3$ $[M+Na]^+$ 352.1637, found: 352.1649; $[\alpha]_D^{20}$ +30.7 (c 1.3, CH_2Cl_2).



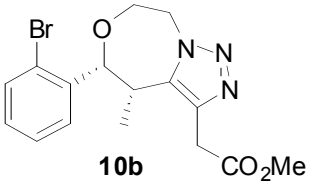
9i

(5*S*, 6*S*)-methyl 6-(2-azidoethoxy)-6-cyclohexyl-5-methylhex-3-ynoate (9i): Same procedure as **9a** using cyclohexanecarboxaldehyde (0.067 g, 0.6 mmol) yields **9i** (0.024 g, 0.078 mmol, 16 % yield). ^{1}H NMR (400 MHz, $CDCl_3$): δ 3.91 (m, 1H), 3.71 (s, 3H), 3.68 (m, 1H), 3.33 (m, 2H), 3.25 (d, J=2.4, 2H), 3.02 (t, J=6.0, 1H), 2.67 (m, 1H), 1.64 (m, 6H), 1.21 (m, 2H), 1.17 (d, J=7.2, 3H), 1.10 (m, 2H); ^{13}C NMR (75 MHz, $CDCl_3$): δ 169.2, 87.8, 86.7, 72.5, 72.0, 52.4, 51.4, 40.8, 30.3, 28.4, 27.8, 26.4, 26.4, 26.2, 25.9, 15.9; IR (film) υ_{max} 2927, 2853, 2104, 1750, 1652, 1456, 1113 cm^{-1}; HRMS(CI, NH_3) m/z calc'd for $C_{16}H_{25}O_3N_3$ $[M+Na]^+$ 330.1794, found: 330.1796; $[\alpha]_D^{20}$ -4.0 (c 1.0, CH_2Cl_2).



10a

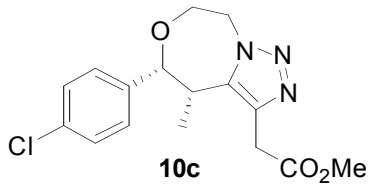
Methyl 2-((4*S*,5*R*)-4-methyl-5-phenyl-4,5,7,8-tertrahydro-[1,2,3]triazolo[1,5-*d*][1,4]oxazepin-3-yl)acetate (10a): A solution of **9a** (0.056 g, 0.186 mmol) in toluene (3 mL) in a sealed tube was heated to 130 ºC and stirred 40 hours. The reaction was cooled to room temperature, and the solvents were removed under vacuum. Purification over silica gel (gradient elution, 95:5 to 80:20 DCM/ethyl acetate) yields **10a** (0.040 g, 0.133 mmol, 71 % yield). ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.36 (m, 4H), 7.28 (m, 1H), 4.86 (m, 1H), 4.76 (s, 1H), 4.62 (m, 1H), 4.44 (m, 1H), 3.85 (m, 1H), 3.76 (dd, J=16.4, 17.6, 2H), 3.72 (s, 3H), 3.33 (m, 1H), 1.10 (d, J=7.2, 3H); ^{13}C NMR (75 MHz, $CDCl_3$): δ 170.6, 140.5, 139.1, 137.8, 128.2, 127.3, 125.5, 83.6, 70.0, 53.0, 52.2, 36.3, 31.2, 11.0; IR (film) υ_{max} 2952, 2871, 1739, 1436, 1243, 1147 cm^{-1}; HRMS(CI, NH_3) m/z calc'd for $C_{16}H_{19}O_3N_3$ $[M+Na]^+$ 324.1324, found: 324.1333; $[\alpha]_D^{20}$ -41.0 (c 1.0, CH_2Cl_2).



10b

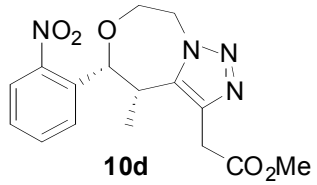
Methyl 2-((4*S*,5*R*)-5-(2-bromophenyl)-4-methyl-4,5,7,8-tertrahydro-[1,2,3]triazolo[1,5-*d*][1,4]oxazepin-3-yl)acetate (10b): Same procedure as **10a** using **9b** (0.144 g, 0.379 mmol) yields **10b** (0.108 g, 0.284 mmol, 75 % yield). ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.55 (m, 2H), 7.35 (t, J=7.6, 1H), 7.16 (t, J=7.6, 1H), 4.86 (t, J=6.8, 2H), 4.62 (m, 1H), 4.43 (m, 1H), 3.85 (m, 2H), 3.71 (d, J=4.0, 1H), 3.66 (s, 3H), 3.45 (m, 1H), 1.13 (d, J=7.2, 3H); ^{13}C NMR (75 MHz, $CDCl_3$): δ 170.4, 139.2, 138.6, 138.0, 132.5, 129.0, 128.4, 127.2, 120.8, 83.0, 70.2, 52.8, 52.1, 33.1, 31.0, 10.9; IR (film) υ_{max} 2950, 2871, 1740, 1436, 1244, 1146 cm^{-1}; HRMS(CI, NH_3) m/z

calc'd for $C_{16}H_{18}O_3N_3Br$ $[M+Na]^+$ 402.0429, found: 402.0439; $[\alpha]_D^{20}$ +126.3 (c 1.1, CH_2Cl_2).



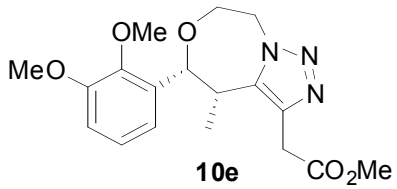
10c

Methyl 2-((4*S*,5*R*)-5-(4-chlorophenyl)-4-methyl-4,5,7,8-tertrahydro-[1,2,3]triazolo[1,5-*d*][1,4]oxazepin-3-yl)acetate (10c): Same procedure as **10a** using **9c** (0.053 g, 0.158 mmol) yields **10c** (0.040 g, 0.119 mmol, 76 % yield). ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.32 (m, 4H), 4.85 (m, 1H), 4.74 (s, 1H), 4.60 (m, 1H), 4.42 (m, 1H) 3.85 (m, 1H), 3.77 (dd, J=16.8, 28.8 2H), 3.71 (s, 3H), 3.31 (m, 1H), 1.07 (d, J=7.2, 3H); ^{13}C NMR (75 MHz, $CDCl_3$): δ 170.6, 139.0, 138.8, 137.8, 133.0, 128.3, 126.9, 82.9, 70.0, 52.9, 52.2, 36.2, 31.1, 10.9; IR (film) υ_{max} 2952, 2859, 1739, 1492, 1436, 1244, 1148 cm^{-1}; HRMS(CI, NH_3) m/z calc'd for $C_{16}H_{18}O_3N_3Cl$ $[M+Na]^+$ 358.0934, found: 358.0923; $[\alpha]_D^{20}$ -85.0 (c 1.0, CH_2Cl_2).



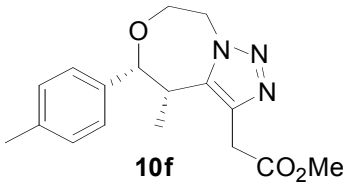
10d

Methyl 2-((4*S*,5*R*)-4-methyl-5-(2-nitrophenyl)-4,5,7,8-tertrahydro-[1,2,3]triazolo[1,5-*d*][1,4]oxazepin-3-yl)acetate (10d): Same procedure as **10a** using **9d** (0.062 g, 0.181 mmol) yields **10d** (0.046 g, 0.119 mmol, 74 % yield). ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.07 (d, J=8.0, 1H), 7.85 (d, J=7.6, 1H), 7.69 (m, 1H), 7.48 (m, 1H), 5.21 (s, 1H), 4.85 (m, 1H), 4.65 (m, 1H), 4.31 (m, 1H), 3.83 (m, 1H), 3.80 (dd, J=16.4, 59.6, 2H), 3.66 (s, 3H), 3.51 (m, 1H), 1.22 (d, J=7.2, 3H); ^{13}C NMR (75 MHz, $CDCl_3$): δ 170.5, 146.4, 138.5, 138.1, 135.9, 133.3, 129.0, 128.5, 124.8, 79.8, 70.3, 52.6, 52.1, 34.4, 31.0, 11.1; IR (film) υ_{max} 2952, 2859, 1740, 1526, 1436, 1341, 1146 cm^{-1}; HRMS(CI, NH_3) m/z calc'd for $C_{16}H_{18}O_5N_4$ $[M+Na]^+$ 369.1175, found: 369.1162; $[\alpha]_D^{20}$ +36.0 (c 1.0, CH_2Cl_2).



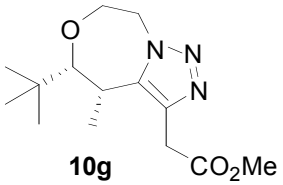
10e

Methyl 2-((4*S*,5*R*)-5-(2,3-dimethoxyphenyl)-4-methyl-4,5,7,8-tertrahydro-[1,2,3]triazolo[1,5-*d*][1,4]oxazepin-3-yl)acetate (10e): Same procedure as **10a** using **9e** (0.118 g, 0.327 mmol) yields **10e** (0.078 g, 0.216 mmol, 66 % yield). ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.09 (m, 2H), 6.86 (m, 1H), 4.86 (s, 1H), 4.82 (m, 1H), 4.60 (m, 1H), 4.41 (m, 1H), 3.87 (s, 3H), 3.83 (m, 1H), 3.80 (s, 3H), 3.73 (dd, J=13.2, 33.6, 2H), 3.67 (s, 3H), 3.39 (m, 1H), 1.08 (d, J=7.2, 3H); ^{13}C NMR (75 MHz, $CDCl_3$): δ 170.3, 152.1, 144.2, 139.3, 138.0, 134.1, 123.6, 118.8, 111.3, 79.5, 70.0, 60.3, 55.6, 52.9, 52.0, 34.2, 30.8, 11.3; IR (film) υ_{max} 2941, 2837, 1741, 1586, 1479, 1275, 1147 cm^{-1}; HRMS(CI, NH_3) m/z calc'd for $C_{18}H_{23}O_5N_3$ $[M+Na]^+$ 384.1535, found: 384.1542; $[\alpha]_D^{20}$ +30.8 (c 1.2, CH_2Cl_2).



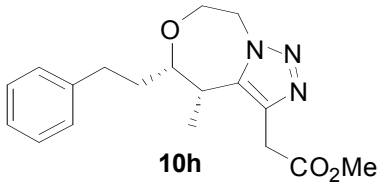
10f

Methyl 2-((4*S*,5*R*)-4-methyl-5-*p*-tolyl-4,5,7,8-tertrahydro-[1,2,3]triazolo[1,5-*d*][1,4]oxazepin-3-yl)acetate (10f): Same procedure as **10a** using **9f** (0.076 g, 0.241 mmol) yields **10f** (0.056 g, 0.176 mmol, 74 % yield). ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.23 (d, J=8.0, 2H), 7.16 (d, J=8.0, 2H), 4.84 (m, 1H), 4.73 (s, 1H), 4.60 (m, 1H), 4.42 (m, 1H), 3.85 (m, 1H), 3.78 (dd, J=8.0, 32.0, 2H), 3.73 (s, 3H), 3.29 (m, 1H), 2.34 (s, 1H), 1.09 (d, J=7.2, 3H); ^{13}C NMR (75 MHz, $CDCl_3$): δ 170.6, 139.1, 137.8, 137.5, 136.9, 128.8, 125.4, 83.6, 70.0, 53.0, 52.2, 36.3, 31.2, 21.0, 11.0; IR (film) υ_{max} 2951, 2863, 1738, 1515, 1435, 1373, 1147 cm^{-1}; HRMS(CI, NH_3) m/z calc'd for $C_{17}H_{21}O_3N_3$ $[M+Na]^+$ 338.1481, found: 338.1474; $[\alpha]_D^{20}$ -70.8 (c 1.2, CH_2Cl_2).



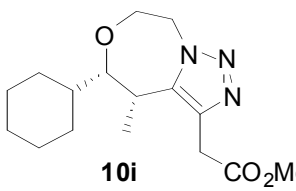
10g

Methyl 2-((4*S*,5*R*)-5-*tert*-butyl-4-methyl-4,5,7,8-tertrahydro-[1,2,3]triazolo[1,5-*d*][1,4]oxazepin-3-yl)acetate (10g): Same procedure as **10a** using **9g** (0.075 g, 0.267 mmol) yields **10g** (0.056 g, 0.199 mmol, 75 % yield). ^{1}H NMR (400 MHz, $CDCl_3$): δ 4.73 (m, 1H), 4.50 (m, 1H), 4.33 (m, 1H), 3.70 (s, 2H), 3.68 (s, 3H), 3.64 (m, 1H), 3.37 (m, 1H), 3.10 (s, 1H), 1.29 (d, J=7.2, 3H), 0.98 (s, 9H); ^{13}C NMR (75 MHz, $CDCl_3$): δ 170.5, 141.1, 136.5, 90.2, 70.9, 53.1, 52.2, 35.8, 31.2, 30.0, 27.4, 13.3; IR (film) υ_{max} 2955, 2869, 1741, 1436, 1362, 1145 cm^{-1}; HRMS(CI, NH_3) m/z calc'd for $C_{14}H_{23}O_3N_3$ $[M+H]^+$ 282.1818, found: 282.1812; $[\alpha]_D^{20}$ -32.5 (c 1.6, CH_2Cl_2).



10h

Methyl 2-((4*S*,5*S*)-4-methyl-5-phenethyl-4,5,7,8-tertrahydro-[1,2,3]triazolo[1,5-*d*][1,4]oxazepin-3-yl)acetate (10h): Same procedure as **10a** using **9h** (0.072 g, 0.218 mmol) yields **10h** (0.041 g, 0.124 mmol, 57 % yield). ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.27 (m, 2H), 7.17 (m, 3H), 4.74 (m, 1H), 4.47 (m, 1H), 4.29 (m, 1H), 3.67 (dd, J=16.8, 15.6 2H), 3.64 (s, 3H), 3.47 (m, 1H), 2.98 (m, 1H), 2.80 (m, 1H), 2.64 (m, 1H), 2.04 (m, 1H), 1.69 (m, 1H), 1.24 (d, J=7.2, 3H); ^{13}C NMR (75 MHz, $CDCl_3$): δ 170.5, 141.4, 139.3, 137.6, 128.5, 128.4, 126.0, 81.6, 69.7, 53.2, 52.2, 35.9, 34.0, 32.3, 31.2, 11.7; IR (film) υ_{max} 2955, 2869, 1733, 1456, 1362, 1145 cm^{-1}; HRMS(CI, NH_3) m/z calc'd for $C_{18}H_{23}O_3N_3$ $[M+Na]^+$ 352.1637, found: 352.1638; $[\alpha]_D^{20}$ -20.5 (c 1.8, CH_2Cl_2).



10i

Methyl 2-((4*S*,5*S*)-5-cyclohexyl-4-methyl-4,5,7,8-tertrahydro-[1,2,3]triazolo[1,5-*d*][1,4]oxazepin-3-yl)acetate (10i): Same procedure as **10a** using **9i** (0.025 g, 0.081 mmol) yields **10i** (0.020 g, 0.065 mmol, 80 % yield). ^{1}H NMR (400 MHz, $CDCl_3$): δ 4.73 (m, 1H), 4.47 (m, 1H), 4.28 (m, 1H), 3.71 (s, 2H), 3.69 (s, 3H), 3.61 (t, J=15.6, 1H), 3.26 (q, J=7.2, 1H), 3.12 (d, J=9.6, 1H), 2.12 (m, 1H), 1.72 (m, 4H), 1.28 (m, 3H), 1.18 (d, J=7.6, 3H), 0.90 (m, 3H); ^{13}C NMR (75 MHz, $CDCl_3$): δ 170.6, 139.6, 137.7, 87.7, 70.1, 53.3, 52.2, 39.7, 31.3, 30.3, 30.1, 29.0, 26.2, 26.0, 25.7, 11.6; IR (film) υ_{max} 2925, 2852, 1741, 1436, 1375, 1140 cm^{-1};

HRMS(CI, NH_3) m/z calc'd for $C_{16}H_{25}O_3N_3$ $[M+H]^+$ 308.1974, found: 308.1975; $[\alpha]_D^{20}$ -35.0 (c 1.0, CH_2Cl_2).

(*S*)-(1-azidopropan-2-yloxy)(*tert*-butyl)dimethylsilane (11a): The vinyl iodide precursor was prepared in 3 steps (TBS protection of the primary alcohol, $LiBH_4$ reduction of the ester, then iodide displacement of the resulting primay alcohol) using known procedures starting with ethyl lactate.[2] This iodide (2.80 g, 9.33 mmol) was dissolved in DMSO (20 mL). Sodium azide (0.91 g, 14.00 mmol) was added, and the solution was stirred for 18 hours at room temperature. The reaction was poured onto water, extracted with ethyl acetate (3 X 10 mL), dried with magnesium sulfate, filtered and the solvents were removed under vacuum. Purification over silica gel (97:3 hexanes/ethyl acetate) yields **11a** (1.81 g, 8.40 mmol, 90 % yield). ^{1}H NMR (400 MHz, $CDCl_3$): δ 3.94 (m, 1H), 3.10 (t, J=3.2, 2H), 1.15 (d, J=6.4, 3H), 0.89 (s, 9H), 0.08 (d, J=6.8, 6H); ^{13}C NMR (75 MHz, $CDCl_3$): δ 68.1, 58.4, 25.7, 21.2, 18.0, -4.7, -4.9; IR (film) υ_{max} 2958, 2859, 2102, 1472, 1257, 1145 cm^{-1}; $[\alpha]_D^{20}$ -5.5 (c 4.5, CH_2Cl_2).[3]

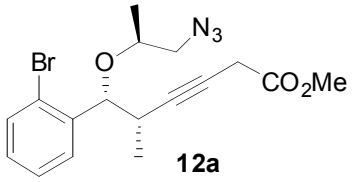
(*S*)-(2-azido-2-phenylethoxy)(*tert*-butyl)dimethylsilane (11b): *R*-styrene oxide (1.0 g, 8.32 mmol) was added to a solution of sodium azide (1.08 g, 16.64 mmol) in water (10 mL) in a sealed tube. The solution was heated to 70 ºC and stirred 12 hours. The product was extracted with ethyl acetate, washed with water, dried with magnesium sulfate, filtered and the solvents were removed under vacuum. The crude product was dissolved in DCM (16 mL), and chilled to 0 ºC. Imidizole (1.13 g, 16.64 mmol) and TBSCl (1.25 g, 9.15 mmol) were added, and the solution was stirred overnight warming from 0 ºC to room temperature. The reaction was quenched with water, and extracted with DCM. The organic layers were washed with water, dried with magnesium sulfate, filtered and the solvents were removed under vacuum. Purification over silica gel (97:3 hexanes/ethyl acetate) yields **11b** (1.56 g, 5.62 mmol, 68 % yield over 2 steps). ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.32 (m, 5H), 4.58 (q, J=3.6, 1H), 3.78 (m, 2H), 0.88 (s, 9H), 0.04 (d, J=7.2, 6H); ^{13}C NMR (75 MHz, $CDCl_3$): δ 137.0, 128.6, 128.2, 127.0, 68.2, 67.4, 25.8, 18.3, -5.5, -5.6; IR (film) υ_{max} 2955, 2858, 2100, 1472, 1258, 1115 cm^{-1}; $[\alpha]_D^{20}$ +60.0 (c 2.5, CH_2Cl_2).[3]

[2] Kraft, P.; Tochtermann, W. *Liebigs Annalen* **1995**, *8*, 1409-1414.

[3] The azido TBS ethers were not stable to mass spec conditions, they decomposed/polymerized without giving reliable readings.

(3-azidopropoxy)(*tert*-butyl)dimethylsilane (11c): 3-bromo-1-propanol (2.78 g, 20 mmol) was dissolved in DCM (20 mL), and chilled to 0 ºC. Imidizole (2.72 g, 40 mmol) and TBSCl (3.31 g, 22 mmol) were added, and the solution was stirred overnight warming from 0 ºC to room temperature. The reaction was quenched with water, and extracted with DCM. The organic layers were washed with water, dried with magnesium sulfate, filtered and the solvents were removed under vacuum. Purification over silica gel (97:3 hexanes/ethyl acetate) yields the TBS ether (4.20 g, 16.58 mmol, 83 % yield) which is spectroscopically identical to reported values (this is commercially available). This ether (4.20 g, 16.58 mmol) was dissolved in DMSO (30 mL). Sodium azide (1.62 g, 24.87 mmol) was added, and the solution was heated to 70 ºC and stirred for 18 hours. The reaction was cooled to room temperature, and poured onto water, extracted with ethyl acetate (3X15 mL), dried with magnesium sulfate, filtered and the solvents were removed under vacuum. Purification over silica gel (97:3 hexanes/ethyl acetate) yields **11c** (2.91 g, 13.51 mmol, 82 % yield). ^{1}H NMR (400 MHz, $CDCl_3$): δ 3.67 (t, J=5.2, 2H), 3.37 (t, J=6.4, 2H), 1.75 (m, 2H), 0.87 (s, 9H), 0.04 (s, 6H); ^{13}C NMR (75 MHz, $CDCl_3$): δ 59.6, 48.2, 31.8, 25.9, 18.3, -5.5; IR (film) υ_{max} 2958, 2859, 2097, 1457, 1436, 1107 cm^{-1}.[3]

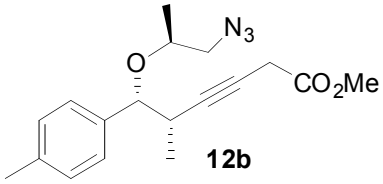
(*R*)-(3-azido-2-methylpropoxy)(*tert*-butyl)dimethylsilane (11d): The same sequence of steps used to make **11a** are used, starting from (*S*)-methyl-3-hydroxy-2-methylpropanpoate (the first 3 steps of this sequence are all previously reported).[4] The final step using the iodide (2.45 g, 7.80 mmol) yields **11d** (1.09 g, 4.75 mmol, 61 % yield). ^{1}H NMR (400 MHz, $CDCl_3$): δ 3.54 (m, 1H), 3.45 (m, 1H), 3.34 (m, 1H), 3.20 (m, 1H), 1.85 (m, 1H), 0.91 (d, J=6.8, 3H), 0.88 (s, 9H), 0.03 (s, 6H); ^{13}C NMR (75 MHz, $CDCl_3$): δ 64.9, 54.3, 36.2, 25.9, 18.3, 14.5, -5.5, -5.5; IR (film) υ_{max} 2957, 2859, 2099, 1472, 1464, 1257, 1100 cm^{-1}; $[\alpha]_D^{20}$ +9.3 (c 2.8, CH_2Cl_2).[3]



12a

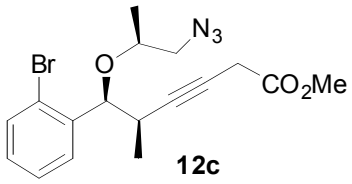
(5*S*, 6*R*)-methyl 6-((*S*)-1-azidopropan-2-yloxy)-6-(2-bromophenyl)-5-methylhex-3-ynoate (12a): Same procedure as **9b** using **11a** (0.108 g, 0.6 mmol) as the silyl ether yields **12a** (0.161 g, 0.408 mmol, 82 % yield). ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.58 (m, 1H), 7.49 (m, 1H), 7.34 (t, J=7.6, 1H), 7.13 (m, 1H), 4.89 (d, J=6.4, 1H), 3.67 (s, 3H), 3.47 (m, 1H), 3.08 (d, J=3.6, 2H), 3.08 (m, 2H), 2.84 (m, 1H), 1.21 (d, J=2.4, 3H), 1.20 (d, J=3.2, 3H); ^{13}C NMR (75 MHz, $CDCl_3$): δ 168.9, 139.3, 132.3, 129.2, 129.1, 127.5, 124.2, 84.5, 79.5, 73.2, 72.3, 56.3, 52.3, 32.7, 25.8, 16.6, 16.3; IR (film) υ_{max} 2977, 2832, 2102, 1748, 1437, 1273, 1121 cm^{-1}; HRMS(CI, NH_3) m/z calc'd for $C_{17}H_{20}O_3N_3Br$ $[M+Na]^+$ 416.0586, found: 416.0573; $[\alpha]_D^{20}$ +18.8 (c 1.7, CH_2Cl_2).

[4] Tan, Z.; Negishi, E. *Angew. Chem. Int. Ed.* **2004**, *43*, 2911-2914.



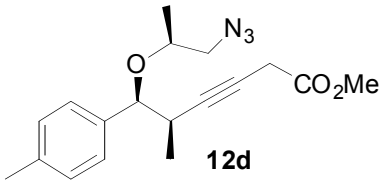
12b

(5*S*, 6*R*)-methyl 6-((*S*)-1-azidopropan-2-yloxy)-5-methyl-6-*p*-tolylhex-3-ynoate (12b): Same procedure as **12a** using *p*-tolualdehyde (0.072 g, 0.6 mmol) yields **12b** (0.102 g, 0.310 mmol, 62 % yield). ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.25 (m, 1H), 7.19 (m, 1H), 7.14 (m, 2H), 4.24 (d, J=7.2, 1H), 3.68 (s, 3H), 3.50 (m, 1H), 3.27 (m, 1H), 3.14 (d, J=2.4, 2H), 3.08 (m, 1H), 2.75 (m, 1H), 2.33 (s, 3H), 1.19 (d, J=6.8, 3H), 1.14 (d, J=6.0, 3H); ^{13}C NMR (75 MHz, $CDCl_3$): δ 169.0, 137.4, 136.9, 128.7, 127.5, 127.5, 85.2, 81.8, 73.4, 71.5, 56.4, 52.3, 33.9, 25.8, 21.1, 17.1, 16.4; IR (film) υ_{max} 2976, 2832, 2102, 1751, 1437, 1272, 1112 cm^{-1}; HRMS(CI, NH_3) m/z calc'd for $C_{18}H_{23}O_3N_3$ $[M+Na]^+$ 352.1637, found: 352.1646; $[\alpha]_D^{20}$ -37.2 (c 1.1, CH_2Cl_2).



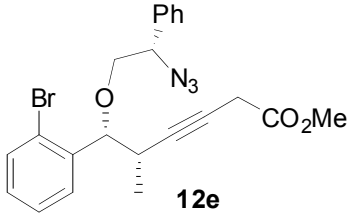
12c

(5*R*, 6*S*)-methyl 6-((*S*)-1-azidopropan-2-yloxy)-6-(2-bromophenyl)-5-methylhex-3-ynoate (12c): Same procedure as **12a** using the **(S_a)-4a** enantiomer of the allenylsilane yields **12c** (0.158 g, 0.401 mmol, 80 % yield). ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.54 (d, J=8.0, 1H), 7.49 (d, J=8.0, 1H), 7.31 (t, J=7.6, 1H), 7.13 (t, J=7.6, 1H), 4.88 (d, J=5.2, 1H), 3.69 (s, 3H), 3.64 (m, 1H), 3.39 (m, 1H), 3.27(m, 1H), 3.22 (d, J=2.0, 2H), 2.86 (m, 1H), 1.16 (d, J=6.8, 3H), 1.01 (d, J=6.4, 3H); ^{13}C NMR (75 MHz, $CDCl_3$): δ 168.9, 140.1, 132.3, 129.3, 129.0, 127.2, 123.2, 84.8, 81.2, 74.5, 73.1, 55.5, 52.3, 32.3, 25.8, 18.4, 15.5; IR (film) υ_{max} 2978, 2832, 2102, 1748, 1437, 1273, 1122 cm^{-1}; HRMS(CI, NH_3) m/z calc'd for $C_{17}H_{20}O_3N_3Br$ $[M+Na]^+$ 416.0586, found: 416.0582; $[\alpha]_D^{20}$ -27.0 (c 1.0, CH_2Cl_2).



12d

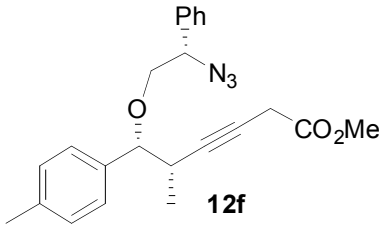
(5*R*, 6*S*)-methyl 6-((*S*)-1-azidopropan-2-yloxy)-5-methyl-6-*p*-tolylhex-3-ynoate (12d): Same procedure as **12b** using the **(S_a)-4a** enantiomer of the allenylsilane yields **12d** (0.135 g, 0.410 mmol, 82 % yield). ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.23 (d, J=8.8, 2H), 7.11 (d, J=7.6, 1H), 4.32 (d, J=6.4, 1H), 3.69 (s, 3H), 3.58 (m, 1H), 3.33 (m, 1H), 3.24 (m, 1H), 3.18 (d, J=2.4, 2H), 2.75 (m, 1H), 2.33 (s, 3H), 1.16 (d, J=6.8, 3H), 1.03 (d, J=6.8, 3H); ^{13}C NMR (75 MHz, $CDCl_3$): δ 169.0, 137.6, 137.2, 128.5, 127.3, 85.2, 83.4, 73.4, 73.3, 55.6, 52.2, 33.8, 25.8, 21.1, 18.7, 16.5; IR (film) υ_{max} 2976, 2833, 2102, 1748, 1437, 1273, 1111 cm^{-1}; HRMS(CI, NH_3) m/z calc'd for $C_{18}H_{23}O_3N_3$ $[M+Na]^+$ 352.1637, found: 352.1651; $[\alpha]_D^{20}$ +76.4 (c 1.7, CH_2Cl_2).



12e

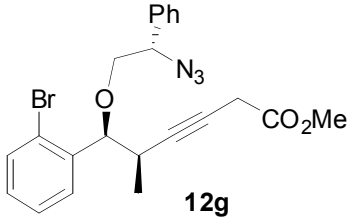
(5*S*, 6*R*)-methyl 6-((*S*)-2-azido-2-phenylethoxy)-6-(2-bromophenyl)-5-methylhex-3-ynoate (12e): Same procedure as **9b** using **11b** (0.166 g, 0.6 mmol) as the silyl ether yields **12e** (0.211 g, 0.462 mmol, 92 % yield). ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.50 (m, 2H), 7.32 (m, 6H), 7.13 (m, 1H), 4.80 (d, J=5.6, 1H), 4.78 (m, 1H), 3.67 (s, 3H), 3.55 (m, 2H), 3.20 (d, J=2.4, 2H), 2.90 (m, 1H), 1.17 (d, J=7.2, 3H); ^{13}C NMR (75

MHz, $CDCl_3$): δ 168.9, 138.5, 136.5, 132.4, 129.2, 128.8, 128.5, 128.2, 127.5, 126.9, 123.9, 84.5, 82.8, 73.6, 73.2, 64.9, 52.3, 32.3, 25.8, 15.8; IR (film) υ_{max} 2978, 2832, 2100, 1751, 1437, 1265, 1112 cm^{-1}; HRMS(CI, NH_3) m/z calc'd for $C_{22}H_{22}O_3N_3Br$ $[M+Na]^+$ 478.0742, found: 478.0748; $[\alpha]_D^{20}$ +55.5 (c 1.8, CH_2Cl_2).



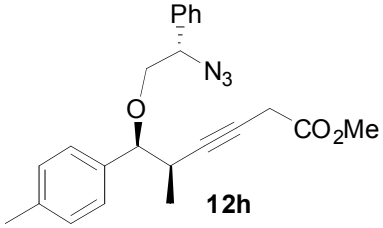
12f

(5*S*, 6*R*)-methyl 6-((*S*)-2-azido-2-phenylethoxy)-5-methyl-6-*p*-tolylhex-3-ynoate (12f): Same procedure as **12e** using *p*-tolualdehyde (0.072 g, 0.6 mmol) yields **12f** (0.158 g, 0.404 mmol, 81 % yield). ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.31 (m, 5H), 7.20 (d, J=8.0, 2H), 7.11 (d, J=8.0, 2H), 4.73 (m, 1H), 4.14 (d, J=6.8, 1H), 3.67 (s, 3H), 3.57 (m, 1H), 3.47 (m, 1H), 3.16 (d, J=2.4, 2H), 2.78 (m, 1H), 2.33 (s, 3H), 1.16 (d, J=6.8, 3H); ^{13}C NMR (75 MHz, $CDCl_3$): δ 169.0, 137.4, 136.7, 136.2, 128.8, 128.5, 128.2, 127.4, 127.4, 127.0, 85.1, 84.9, 73.5, 73.0, 65.0, 52.3, 33.7, 25.8, 21.1, 16.8; IR (film) υ_{max} 2951, 2832, 2100, 1748, 1436, 1266, 1112 cm^{-1}; HRMS(CI, NH_3) m/z calc'd for $C_{23}H_{25}O_3N_3$ $[M+Na]^+$ 414.1794, found: 414.1806; $[\alpha]_D^{20}$ +63.8 (c 1.3, CH_2Cl_2).



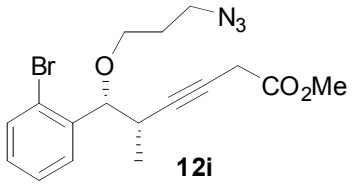
12g

(5*R*, 6*S*)-methyl 6-((*S*)-2-azido-2-phenylethoxy)-6-(2-bromophenyl)-5-methylhex-3-ynoate (12g): Same procedure as **12e** using the **(S_a)-4a** enantiomer of the allenylsilane yields **12g** (0.210 g, 0.460 mmol, 92 % yield). ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.48 (m, 1H), 7.40 (m, 1H), 7.32 (m, 5H), 7.13 (m, 2H), 4.82 (d, J=6.4, 1H), 4.62 (m, 1H), 3.67 (s, 3H), 3.53 (m, 2H), 3.18 (d, J=2.4, 2H), 2.89 (m, 1H), 1.21 (d, J=7.6, 3H); ^{13}C NMR (75 MHz, $CDCl_3$): δ 168.9, 138.8, 136.6, 132.5, 129.2, 128.7, 128.5, 128.3, 127.4, 127.0, 123.9, 84.4, 83.2, 73.6, 73.3, 65.3, 52.3, 32.5, 25.8, 16.1; IR (film) υ_{max} 2979, 2906, 2101, 1747, 1436, 1266, 1111 cm^{-1}; HRMS(CI, NH_3) m/z calc'd for $C_{22}H_{22}O_3N_3Br$ $[M+Na]^+$ 478.0742, found: 478.0740; $[\alpha]_D^{20}$ +3.8 (c 4.8, CH_2Cl_2).



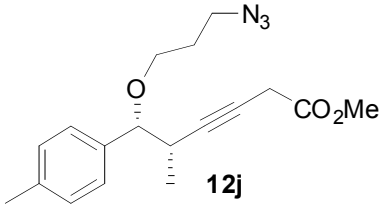
12h

(5*R*, 6*S*)-methyl 6-((*S*)-2-azido-2-phenylethoxy)-5-methyl-6-*p*-tolylhex-3-ynoate (12h): Same procedure as **12f** using the **(S_a)-4a** enantiomer of the allenylsilane yields **12h** (0.156 g, 0.399 mmol, 80 % yield). ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.30 (m, 5H), 7.17 (d, J=8.0, 2H), 7.09 (d, J=8.0, 2H), 4.63 (m, 1H), 4.18 (d, J=7.2, 1H), 3.67 (s, 3H), 3.50 (m, 2H), 3.15 (d, J=2.0, 2H), 2.81 (m, 1H), 2.31 (s, 3H), 1.23 (d, J=6.8, 3H); ^{13}C NMR (75 MHz, $CDCl_3$): δ 169.0, 137.4, 136.7, 136.4, 128.6, 128.5, 128.2, 127.4, 126.9, 85.6, 84.9, 73.6, 73.2, 65.5, 52.2, 33.7, 25.8, 21.1, 17.2; IR (film) υ_{max} 2975, 2832, 2100, 1749, 1455, 1265, 1110 cm^{-1}; HRMS(CI, NH_3) m/z calc'd for $C_{23}H_{25}O_3N_3$ $[M+Na]^+$ 414.1794, found: 414.1783; $[\alpha]_D^{20}$ +24.7 (c 1.7, CH_2Cl_2).



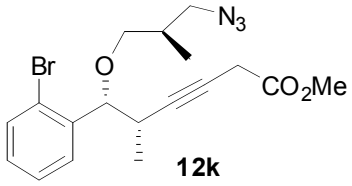
12i

(5*S*, 6*R*)-methyl 6-(3-azidopropoxy)-6-(2-bromophenyl)-5-methylhex-3-ynoate (12i): Same procedure as **9b** using **11c** (0.129 g, 0.6 mmol) as the silyl ether yields **12i** (0.170 g, 0.431 mmol, 86 % yield). ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.52 (m, 2H), 7.33 (m, 1H), 7.13 (m, 1H), 4.72 (d, J=5.6, 1H), 3.68 (s, 3H), 3.40 (m, 4H), 3.19 (d, J=2.4, 2H), 2.86 (m, 1H), 1.81 (m, 2H), 1.16 (d, J=6.8, 3H); ^{13}C NMR (75 MHz, $CDCl_3$): δ 168.9, 139.1, 132.4, 129.0, 128.6, 127.3, 123.9, 84.7, 81.3, 73.0, 66.0, 52.3, 48.4, 32.3, 29.1, 25.7, 16.0; IR (film) υ_{max} 2953, 2873, 2097, 1749, 1436, 1264, 1109 cm^{-1}; HRMS(CI, NH_3) m/z calc'd for $C_{17}H_{20}O_3N_3Br$ $[M+Na]^+$ 416.0586, found: 416.0571; $[\alpha]_D^{20}$ +48.7 (c 2.4, CH_2Cl_2).



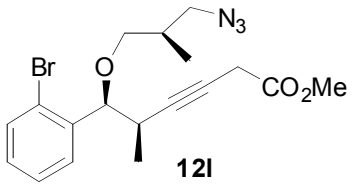
12j

(5*S*, 6*R*)-methyl 6-(3-azidopropoxy)-5-methyl-6-*p*-tolylhex-3-ynoate (12j): Same procedure as **12i** using *p*-tolualdehyde (0.072 g, 0.6 mmol) yields **12j** (0.109 g, 0.331 mmol, 66 % yield). ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.19 (d, J=8.0, 2H), 7.12 (d, J=8.0, 1H), 4.08 (d, J=6.8, 1H), 3.68 (s, 3H), 3.38 (m, 4H), 3.16 (d, J=2.4, 2H), 2.74 (m, 1H), 2.33 (s, 3H), 1.79 (m, 2H), 1.17 (d, J=7.2, 3H); ^{13}C NMR (75 MHz, $CDCl_3$): δ 169.0, 137.2, 136.9, 128.6, 127.3, 85.2, 84.8, 73.4, 65.7, 52.3, 48.5, 33.7, 28.2, 25.8, 21.1, 17.0; IR (film) υ_{max} 2952, 2874, 2107, 1750, 1436, 1265, 1109 cm^{-1}; HRMS(CI, NH_3) m/z calc'd for $C_{18}H_{23}O_3N_3$ $[M+Na]^+$ 352.1637, found: 352.1640; $[\alpha]_D^{20}$ +25.0 (c 1.0, CH_2Cl_2).



12k

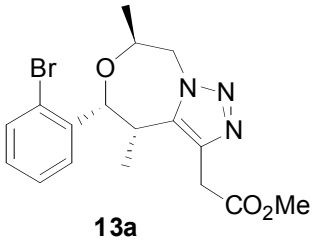
(5*S*, 6*R*)-methyl 6-((*R*)-3-azido-2-methylpropoxy)-6-(2-bromophenyl)-5-methylhex-3-ynoate (12k): Same procedure as **9b** using **11d** (0.138 g, 0.6 mmol) as the silyl ether yields **12k** (0.126 g, 0.309 mmol, 62 % yield). ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.50 (m, 1H), 7.42 (m, 1H), 7.32 (t, J=6.4, 1H), 7.13 (m, 1H), 4.70 (d, J=6.0, 1H), 3.68 (s, 3H), 3.43 (m, 1H), 3.22 (m, 5H), 2.85 (m, 1H), 1.99 (m, 1H), 1.16 (d, J=6.8, 3H), 0.93 (d, J=6.8, 3H); ^{13}C NMR (75 MHz, $CDCl_3$): δ 169.0, 139.2, 132.5, 129.0, 128.7, 127.3, 124.0, 84.8, 82.5, 73.0, 71.4, 54.5, 52.3, 34.1, 32.4, 25.8, 16.0, 14.8; IR (film) υ_{max} 2954, 2876, 2099, 1749, 1436, 1267, 1162 cm^{-1}; HRMS(CI, NH_3) m/z calc'd for $C_{18}H_{22}O_3N_3Br$ $[M+Na]^+$ 430.0742, found: 430.0731; $[\alpha]_D^{20}$ +46.8 (c 1.9, CH_2Cl_2).



12l

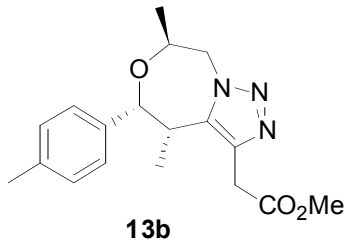
(5*R*, 6*S*)-methyl 6-((*R*)-3-azido-2-methylpropoxy)-6-(2-bromophenyl)-5-methylhex-3-ynoate (12l): Same procedure as **12k** using the **(S_a)-4a** enantiomer of the allenylsilane yields **12l** (0.145 g, 0.355 mmol, 71 % yield). ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.50 (m, 1H), 7.43 (m, 1H), 7.33 (t, J=7.2, 1H), 7.13 (m, 1H), 4.69 (d, J=6.0, 1H), 3.68 (s, 3H), 3.40 (m, 1H), 3.26 (m, 5H), 2.85 (m, 1H), 1.95 (m, 1H), 1.17 (d, J=7.2, 3H), 0.94 (d, J=6.8, 3H); ^{13}C NMR (75 MHz, $CDCl_3$): δ 168.9, 139.2, 132.5, 129.0, 128.6, 127.3, 123.9, 84.8, 82.7, 73.0, 71.6,

54.5, 52.3, 34.3, 32.4, 25.8, 16.0, 14.7; IR (film) υ_{max} 2955, 2877, 2099, 1750, 1437, 1267, 1167 cm^{-1}; HRMS(CI, NH_3) m/z calc'd for $C_{18}H_{22}O_3N_3Br$ $[M+Na]^+$ 430.0742, found: 430.0733; $[\alpha]_D^{20}$ +45.3 (c 1.3, CH_2Cl_2).



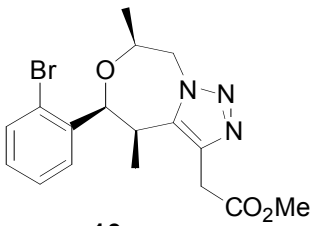
13a

Methyl 2-((4*S*,5*R*,7*S*)-5-(2-bromophenyl)-4,7-dimethyl-4,5,7,8-tertrahydro-[1,2,3]triazolo[1,5-*d*][1,4]oxazepin-3-yl)acetate (13a): Same procedure as **10a** using **12a** (0.085 g, 0.216 mmol) yields **13a** (0.054 g, 0.137 mmol, 64 % yield). ^1H NMR (400 MHz, $CDCl_3$): δ 7.57 (m, 2H), 7.35 (t, J=7.2, 1H), 7.16 (m, 1H), 5.22 (s, 1H), 4.81 (m, 1H), 4.69 (m, 1H), 4.60 (m, 1H), 3.79 (dd, J=16.8, 50.0, 2H), 3.66 (s, 3H), 3.43 (m, 1H), 1.15 (d, J=7.2, 3H), 1.13 (d, J=7.6, 3H); ^{13}C NMR (75 MHz, $CDCl_3$): δ 170.5, 139.5, 138.1, 138.0, 132.6, 129.0, 128.8, 127.2, 121.3, 77.2, 72.4, 70.4, 55.8, 52.2, 32.6, 31.1, 14.2, 10.1; IR (film) υ_{max} 2979, 2950, 1742, 1436, 1244, 1170 cm^{-1}; HRMS(CI, NH_3) m/z calc'd for $C_{17}H_{20}O_3N_3Br$ $[M+H]^+$ 394.0766, found: 394.0768; $[\alpha]_D^{20}$ +53.5 (c 1.6, CH_2Cl_2).



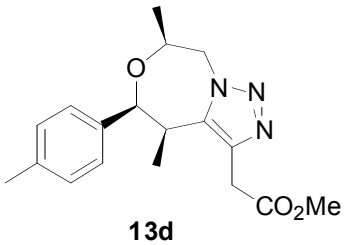
13b

Methyl 2-((4*S*,5*R*,7*S*)-4,7-dimethyl-5-*p*-tolyl-4,5,7,8-tertrahydro-[1,2,3]triazolo[1,5-*d*][1,4]oxazepin-3-yl)acetate (13b): Same procedure as **10a** using **12b** (0.066 g, 0.200 mmol) yields **13b** (0.037 g, 0.112 mmol, 56 % yield). ^1H NMR (400 MHz, $CDCl_3$): δ 7.22 (m, 2H), 7.16 (m, 2H), 5.08 (s, 1H), 4.74 (m, 2H), 4.57 (m, 1H), 3.77 (dd, J=19.2, 15.2, 2H), 3.71 (s, 3H), 3.23 (m, 1H), 2.33 (s, 1H), 1.13 (d, J=6.8, 3H), 1.11 (d, J=7.6, 3H); ^{13}C NMR (75 MHz, $CDCl_3$): δ 170.6, 138.7, 137.9, 137.8, 136.9, 128.8, 125.8, 83.7, 72.9, 70.1, 56.0, 52.3, 35.9, 31.2, 21.0, 14.3, 10.3; IR (film) υ_{max} 2978, 2863, 1740, 1515, 1437, 1384, 1171 cm^{-1}; HRMS(CI, NH_3) m/z calc'd for $C_{18}H_{23}O_3N_3$ $[M+Na]^+$ 352.1637, found: 352.1645; $[\alpha]_D^{20}$ -31.0 (c 1.0, CH_2Cl_2).



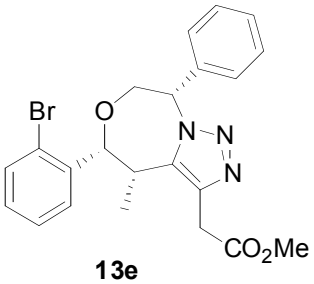
13c

Methyl 2-((4*R*,5*S*,7*S*)-5-(2-bromophenyl)-4,7-dimethyl-4,5,7,8-tertrahydro-[1,2,3]triazolo[1,5-*d*][1,4]oxazepin-3-yl)acetate (13c): Same procedure as **10a** using **12c** (0.143 g, 0.363 mmol) yields **13c** (0.104 g, 0.264 mmol, 73 % yield). ^1H NMR (400 MHz, $CDCl_3$): δ 7.59 (d, J=6.8, 1H), 7.52 (d, J=8.0, 1H), 7.35 (t, J=7.6, 1H), 7.16 (t, J=7.6, 1H), 4.93 (s, 1H), 4.82 (d, J=14.4, 1H), 4.37 (m, 1H), 4.00 (m, 1H), 3.77 (dd, J=16.8, 50.8, 2H), 3.66 (s, 3H), 3.45 (m, 1H), 1.41 (d, J=6.4, 3H), 1.12 (d, J=7.6, 3H); ^{13}C NMR (75 MHz, $CDCl_3$): δ 170.4, 139.6, 138.7, 137.9, 132.5, 129.0, 128.6, 127.1, 120.8, 82.0, 76.4, 57.7, 52.1, 32.9, 30.9, 20.0, 10.9; IR (film) υ_{max} 2981, 2936, 1742, 1436, 1247, 1155 cm^{-1}; HRMS(CI, NH_3) m/z calc'd for $C_{17}H_{20}O_3N_3Br$ $[M+Na]^+$ 416.0586, found: 416.0578; $[\alpha]_D^{20}$ -115.8 (c 1.2, CH_2Cl_2).



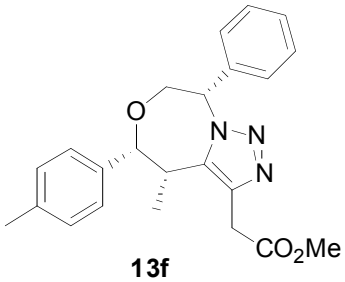
13d

Methyl 2-((4*R*,5*S*,7*S*)-4,7-dimethyl-5-*p*-tolyl-4,5,7,8-tertrahydro-[1,2,3]triazolo[1,5-*d*][1,4]oxazepin-3-yl)acetate (13d): Same procedure as **10a** using **12d** (0.121 g, 0.367 mmol) yields **13d** (0.100 g, 0.303 mmol, 83 % yield). ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.25 (d, J=8.0, 2H), 7.15 (d, J=8.0, 2H), 4.80 (m, 2H), 4.34 (m, 1H), 3.96 (m, 1H), 3.75 (dd, J=16.4, 11.2, 2H), 3.70 (s, 3H), 3.27 (m, 1H), 2.33 (s, 1H), 1.42 (d, J=6.8, 3H), 1.07 (d, J=7.2, 3H); ^{13}C NMR (75 MHz, $CDCl_3$): δ 170.6, 139.2, 137.9, 136.8, 128.8, 125.5, 82.5, 76.1, 58.0, 52.2, 36.1, 31.1, 21.0, 19.8, 11.0; IR (film) υ_{max} 2979, 2934, 1740, 1436, 1375, 1155 cm^{-1}; HRMS(CI, NH_3) m/z calc'd for $C_{18}H_{23}O_3N_3$ $[M+H]^+$ 330.1818, found: 330.1812; $[\alpha]_D^{20}$ +6.0 (c 2.5, CH_2Cl_2).



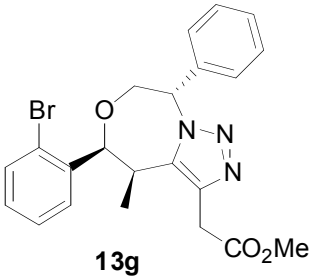
13e

Methyl 2-((4*S*,5*R*,8*S*)-5-(2-bromophenyl)-4-methyl-8-phenyl-4,5,7,8-tertrahydro-[1,2,3]triazolo[1,5-*d*][1,4]oxazepin-3-yl)acetate (13e): Same procedure as **10a** using **12e** (0.137 g, 0.300 mmol) yields **13e** (0.092 g, 0.202 mmol, 67 % yield). ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.51 (m, 2H), 7.38 (m, 6H), 7.14 (m, 1H), 6.16 (s, 1H), 5.17 (dd, J=2.4, 7.2, 1H), 4.99 (s, 1H), 4.28 (dd, J=2.0, 12.0, 1H), 3.77 (dd, J=16.8, 31.6, 2H), 3.67 (s, 3H), 3.43 (m, 1H), 0.50 (d, J=7.6, 3H); ^{13}C NMR (75 MHz, $CDCl_3$): δ 170.3, 139.0, 138.5, 138.4, 136.6, 132.5, 129.1, 128.7, 128.6, 127.9, 127.1, 126.7, 120.7, 84.1, 71.4, 65.0, 52.2, 33.2, 31.2, 11.8; IR (film) υ_{max} 2979, 2951, 1743, 1436, 1243, 1120 cm^{-1}; HRMS(CI, NH_3) m/z calc'd for $C_{22}H_{22}O_3N_3Br$ $[M+H]^+$ 456.0923, found: 456.0920; $[\alpha]_D^{20}$ +69.0 (c 3.0, CH_2Cl_2).



13f

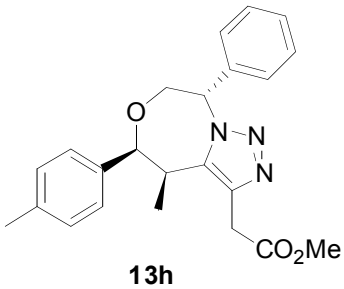
Methyl 2-((4*S*,5*R*,8*S*)-4-methyl-8-phenyl-5-*p*-tolyl-4,5,7,8-tertrahydro-[1,2,3]triazolo[1,5-*d*][1,4]oxazepin-3-yl)acetate (13f): Same procedure as **10a** using **12f** (0.118 g, 0.301 mmol) yields **13f** (0.066 g, 0.169 mmol, 56 % yield). ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.33 (m, 4H), 7.17 (m, 5H), 6.17 (s, 1H), 5.17 (dd, J=1.6, 8.0, 1H), 4.83 (s, 1H), 4.25 (dd, J=1.6, 7.6, 1H), 3.76 (dd, J=16.8, 35.6, 2H), 3.71 (s, 3H), 3.24 (m, 1H), 2.31 (s, 1H), 0.47 (d, J=7.2, 3H); ^{13}C NMR (75 MHz, $CDCl_3$): δ 170.6, 139.1, 138.3, 137.3, 137.0, 136.7, 128.8, 128.6, 128.6, 127.9, 126.8, 125.5, 84.7, 77.2, 71.2, 65.1, 52.3, 36.6, 31.3, 21.0, 11.6; IR (film) υ_{max} 2923, 2863, 1740, 1558, 1457, 1243, 1124 cm^{-1}; HRMS(CI, NH_3) m/z calc'd for $C_{13}H_{25}O_3N_3$ $[M+Na]^+$ 414.1794, found: 414.1783; $[\alpha]_D^{20}$ -4.0 (c 2.5, CH_2Cl_2).



13g

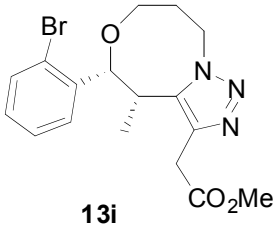
Methyl 2-((4*R*,5*S*,8*S*)-5-(2-bromophenyl)-4-methyl-8-phenyl-4,5,7,8-tertrahydro-[1,2,3]triazolo[1,5-*d*][1,4]oxazepin-3-yl)acetate (13g): Same procedure as **10a** using **12g** (0.167 g, 0.366 mmol) yields **13g** (0.115 g, 0.252 mmol, 69 % yield). ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.56 (m,

2H), 7.38 (m, 6H), 7.18 (m, 1H), 5.73 (d, J=10.0, 1H), 5.04 (s, 1H), 4.36 (dd, J=2.0, 11.6, 1H), 4.18 (m, 1H), 3.79 (dd, J=16.8, 41.2, 2H), 3.66 (s, 3H), 3.57 (m, 1H), 1.22 (d, J=7.2, 3H); ^{13}C NMR (75 MHz, $CDCl_3$): δ 170.5, 139.1, 138.6, 138.1, 133.1, 132.7, 129.1, 129.1, 128.9, 128.8, 128.5, 127.2, 121.0, 82.7, 75.7, 68.2, 52.1, 33.5, 31.1, 11.4; IR (film) υ_{max} 3034, 2951, 1741, 1436, 1235, 1141 cm^{-1}; HRMS(CI, NH_3) m/z calc'd for $C_{22}H_{22}O_3N_3Br$ $[M+H]^+$ 456.0923, found: 456.0927; $[\alpha]_D^{20}$ +20.6 (c 1.5, CH_2Cl_2).



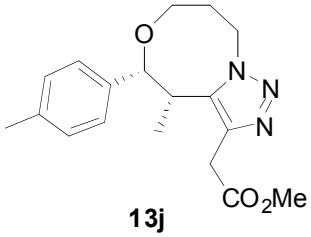
13h

Methyl 2-((4*R*,5*S*,8*S*)-4-methyl-8-phenyl-5-*p*-tolyl-4,5,7,8-tertrahydro-[1,2,3]triazolo[1,5-*d*][1,4]oxazepin-3-yl)acetate (13h): Same procedure as **10a** using **12h** (0.140 g, 0.358 mmol) yields **13h** (0.081 g, 0.207 mmol, 58 % yield). ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.43 (m, 3H), 7.34 (m, 2H), 7.25 (m, 2H), 7.17(m, 2H), 5.71 (dd, J=1.6, 8.8, 1H), 4.90 (s, 1H), 4.36 (dd, J=2.0, 7.6, 1H), 4.16 (m, 1H), 3.77 (dd, J=16.8, 28.0, 2H), 3.71 (s, 3H), 3.43 (m, 1H), 2.35 (s, 1H), 1.17 (d, J=7.2, 3H); ^{13}C NMR (75 MHz, $CDCl_3$): δ 170.7, 139.0, 137.9, 137.3, 137.1, 133.6, 129.0, 128.9, 128.8, 128.8, 125.5, 83.3, 75.4, 68.3, 52.2, 36.6, 31.3, 21.0, 11.5; IR (film) υ_{max} 2923, 2863, 1734, 1652, 1457, 1243, 1124 cm^{-1}; HRMS(CI, NH_3) m/z calc'd for $C_{13}H_{25}O_3N_3$ $[M+Na]^+$ 414.1794, found: 414.1798; $[\alpha]_D^{20}$ +80.0 (c 1.9, CH_2Cl_2).



13i

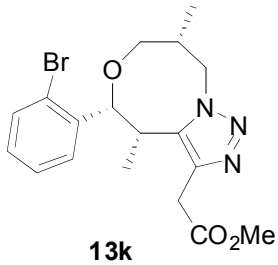
Methyl 2-((4*S*,5*R*)-5-(2-bromophenyl)-4-methyl-5,7,8,9-tertrahydro-4*H*-[1,2,3]triazolo[5,1-*d*][1,5]oxazocin-3-yl)acetate (13i): A solution of **12i** (0.136 g, 0.345 mmol) in chlorobenzene (3 mL) in a sealed tube is heated to 150 ºC and stirred 40 hours. The reaction is cooled to room temperature, and the solvents are removed under vacuum. Purification over silica gel (gradient elution, 95:5 to 80:20 DCM/ethyl acetate) yields **13i** (0.081 g, 0.205 mmol, 60 % yield). ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.51 (m, 2H), 7.32 (t, J=7.6, 1H), 7.15 (t, J=7.2, 1H), 4.86 (t, J=6.8, 2H), 4.83 (d, J=2.4, 1H), 4.71 (m, 2H), 4.22 (m, 1H), 3.77 (dd, J=17.2, 24.4, 2H), 3.66 (s, 3H), 3.63 (m, 1H), 3.01 (m, 1H), 2.27 (m, 1H), 2.08 (m, 1H), 1.10 (d, J=7.6, 3H); ^{13}C NMR (75 MHz, $CDCl_3$): δ 170.7, 139.3, 138.0, 137.3, 132.6, 129.2, 129.1, 127.3, 120.9, 85.7, 77.2, 69.2, 52.2, 46.1, 32.7, 31.4, 31.2, 11.0; IR (film) υ_{max} 2926, 2871, 1741, 1436, 1243, 1197 cm^{-1}; HRMS(CI, NH_3) m/z calc'd for $C_{17}H_{20}O_3N_3Br$ $[M+Na]^+$ 416.0586, found: 416.0598; $[\alpha]_D^{20}$ +44.0 (c 1.0, CH_2Cl_2).



13j

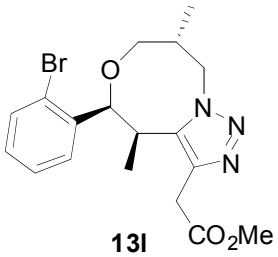
Methyl 2-((4*S*,5*R*)-4-methyl-5-*p*-tolyl-5,7,8,9-tertrahydro-4*H*-[1,2,3]triazolo[5,1-*d*][1,5]oxazocin-3-yl)acetate (13j): Same procedure as **13i** using **12j** (0.101 g, 0.307 mmol) yields **13j** (0.056 g, 0.170 mmol, 55 % yield). ^{1}H NMR (400 MHz,

$CDCl_3$): δ 7.12 (d, J=8.0, 2H), 7.07 (d, J=8.0, 2H), 4.75 (m, 1H), 4.67 (d, J=3.2, 1H), 4.60 (m, 1H), 4.24 (m, 1H), 3.72 (m, 1H), 3.67 (s, 3H), 3.42 (m, 1H), 3.19 (m, 2H), 2.33 (s, 1H), 2.27 (m, 1H), 2.04 (m, 1H), 1.10 (d, J=7.2, 3H); ^{13}C NMR (75 MHz, $CDCl_3$): δ 170.9, 137.9, 137.1, 136.5, 128.7, 126.1, 86.1, 72.2, 68.8, 52.2, 46.8, 35.1, 31.6, 21.1, 11.8; IR (film) υ_{max} 2950, 2863, 1742, 1467, 1436, 1244, 1198 cm^{-1}; HRMS(CI, NH_3) m/z calc'd for $C_{18}H_{23}O_3N_3$ $[M+Na]^+$ 352.1637, found: 352.1635; $[\alpha]_D^{20}$ -26.5 (c 2.0, CH_2Cl_2).



13k

Methyl 2-((4*S*,5*R*,8*R*)-5-(2-bromophenyl)-4,8-dimethyl-5,7,8,9-tertrahydro-4*H*-[1,2,3]triazolo[5,1-*d*][1,5]oxazocin-3-yl)acetate (13k): Same procedure as **13i** using **12k** (0.083 g, 0.203 mmol) yields **13k** (0.060 g, 0.147 mmol, 72 % yield). ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.51 (d, J=8.0, 2H), 7.33 (t, J=7.6, 1H), 7.15 (t, J=7.6, 1H), 4.81 (s, 1H), 4.69 (m, 1H), 4.33 (t, J=12.0, 1H), 3.94 (d, J=12.0, 1H), 3.82 (m, 2H), 3.67 (s, 3H), 3.63 (m, 1H), 3.11 (m, 1H), 2.31 (m, 1H), 1.21 (d, J=6.8, 3H), 1.08 (d, J=7.6, 3H); ^{13}C NMR (75 MHz, $CDCl_3$): δ 170.6, 139.3, 137.9, 137.3, 132.5, 129.1, 129.0, 127.2, 120.7, 85.3, 77.2, 74.5, 52.2, 51.9, 36.8, 32.4, 31.3, 29.6, 16.1, 10.8; IR (film) υ_{max} 2961, 2871, 1742, 1436, 1247, 1198 cm^{-1}; HRMS(CI, NH_3) m/z calc'd for $C_{18}H_{22}O_3N_3Br$ $[M+H]^+$ 408.0923, found: 408.0913; $[\alpha]_D^{20}$ +36.1 (c 1.8, CH_2Cl_2).



13l

Methyl 2-((4*R*,5*S*,8*R*)-5-(2-bromophenyl)-4,8-dimethyl-5,7,8,9-tertrahydro-4*H*-[1,2,3]triazolo[5,1-*d*][1,5]oxazocin-3-yl)acetate (13l): Same procedure as **13i** using **12l** (0.125 g, 0.306 mmol) yields **13l** (0.085 g, 0.208 mmol, 68 % yield). ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.51 (m, 2H), 7.34 (t, J=7.6, 1H), 7.16 (m, 1H), 4.82 (m, 2H), 4.47 (dd, J=2.4, 11.6, 1H), 4.08 (dd, J=2.4, 6.0, 1H), 3.77 (dd, J=17.2, 26.0, 2H), 3.66 (s, 3H), 3.65 (m, 1H), 2.63 (t, J=12.0, 1H), 2.50 (m, 1H), 1.09 (d, J=7.2, 3H), 0.94 (d, J=6.8, 3H); ^{13}C NMR (75 MHz, $CDCl_3$): δ 170.7, 139.1, 137.9, 137.1, 132.5, 129.2, 129.0, 127.2, 120.9, 85.3, 75.4, 52.2, 51.8, 35.7, 32.7, 31.4, 13.4, 11.0; IR (film) υ_{max} 2961, 2878, 1742, 1436, 1246, 1198 cm^{-1}; HRMS(CI, NH_3) m/z calc'd for $C_{18}H_{22}O_3N_3Br$ $[M+H]^+$ 408.0923, found: 408.0914; $[\alpha]_D^{20}$ -22.5 (c 1.2, CH_2Cl_2).