

## Supplementary Information

### C-H Functionalization Enabled Stereoselective Ugi-azide Reaction to $\alpha$ -tetrazolyl Alicyclic Amines

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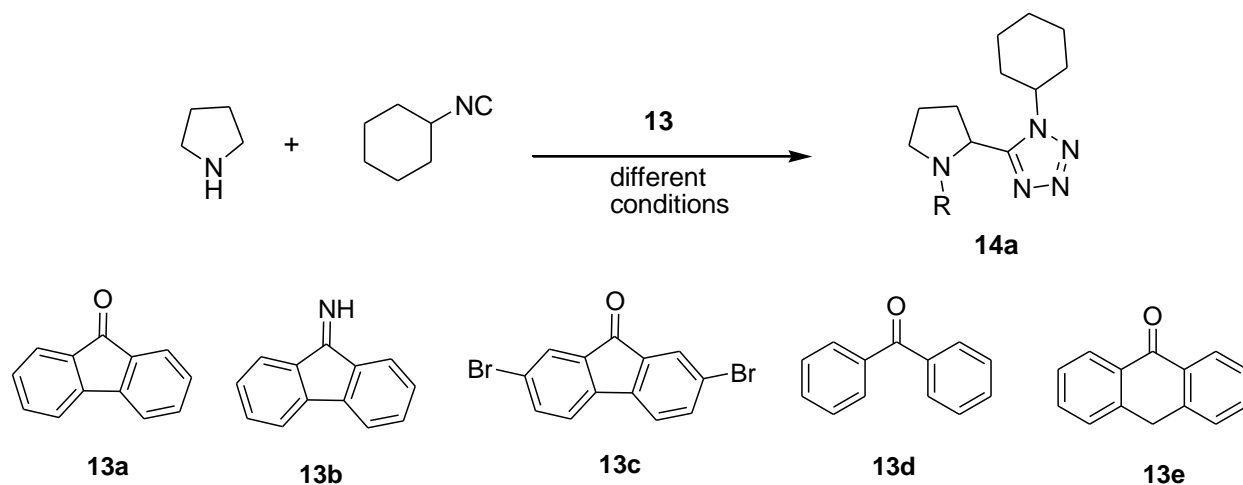
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#### Experimental Section:

**General:** All reactions involving air- or moisture-sensitive reagents or intermediates were carried out in oven-dried glassware under an argon atmosphere. Dichloromethane ( $\text{CH}_2\text{Cl}_2$ ) was freshly distilled from phosphorus(V)oxide ( $\text{P}_2\text{O}_5$ ). Triethylamine ( $\text{Et}_3\text{N}$ ) was distilled from  $\text{CaH}_2$  and stored under argon. Commercial grade xylene, benzene and toluene were distilled before use. All other solvents and reagents were purified according to standard procedures or were used as received from Aldrich, Acros, Merck and Spectrochem.  $^1\text{H}$ ,  $^{13}\text{C}$  NMR spectroscopy: Varian Mercury plus 400 MHz, Bruker 400, 600 MHz (at 298 K). Chemical shifts,  $\delta$  (in ppm), are reported relative to TMS ( $^1\text{H}$ ) 0.0 ppm,  $\delta$  ( $^{13}\text{C}$ ) 0.0 ppm) which was used as the inner reference. Otherwise the solvents residual proton resonance and carbon resonance ( $\text{CHCl}_3$ ,  $\delta$  ( $^1\text{H}$ ) 7.26 ppm,  $\delta$  ( $^{13}\text{C}$ ) 77.2 ppm;  $\text{CD}_3\text{OD}$ , ( $^1\text{H}$ ) 3.31 ppm,  $\delta$  ( $^{13}\text{C}$ ) 49.0 ppm) were used for calibration. Column chromatography: Merck or Spectrochem silica gel 60-120 under gravity. IR: spectra were recorded on Perkin Elmer Instrument at normal temperature making KBr pellet grinding the sample with KBr (IR Grade). MS (ESI-HRMS): Mass spectra were recorded on an Agilent Accurate-Mass Q-TOF LC/MS 6520, and peaks are given in m/z (% of basis peak). HPLC: Waters analytical HPLC, thermo scientific ultimate 3000 /visible detector. Polarimetry: Rudolph research analytical auto plot II.

**Table S1: Additional screened conditions<sup>a</sup>**

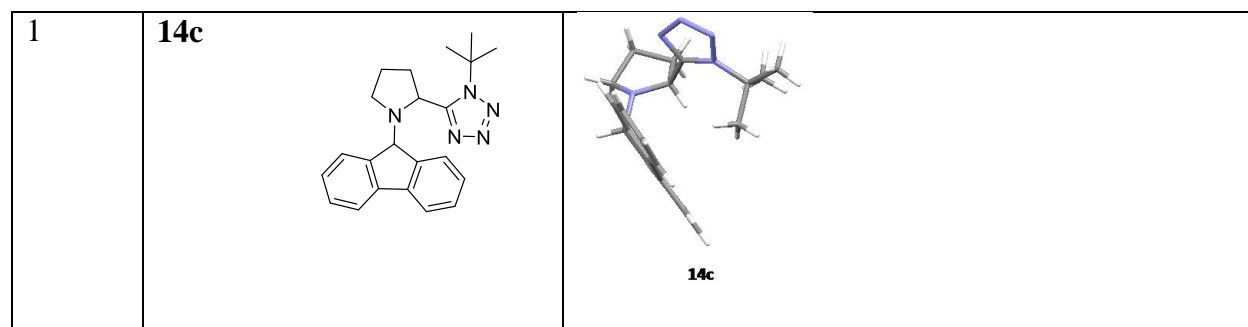


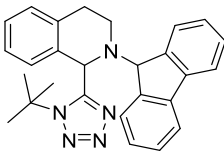
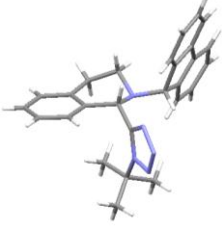
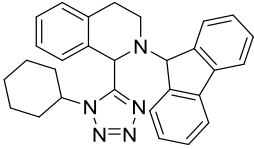
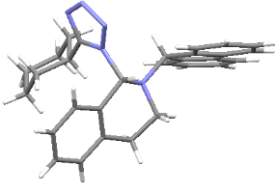
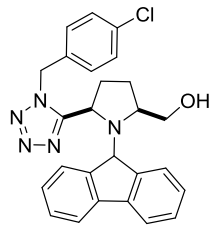
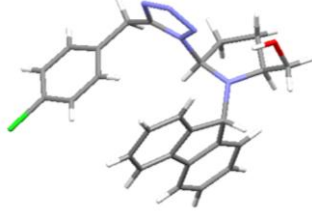
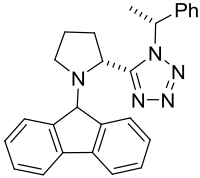
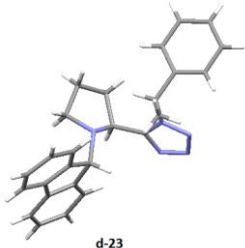
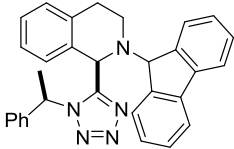
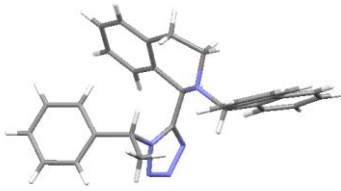
Entry	activators	conditions	Yield <sup>b</sup> (%)
1	<b>13a</b>	TMSN <sub>3</sub> , MeOH, 90 °C, 12 h	85
2	<b>13a</b>	TMSN <sub>3</sub> , MeOH, 90 °C, 24 h	98
3	<b>13a</b>	TMSN <sub>3</sub> , MeOH, rt, 24 h	44
4	<b>13b</b>	TMSN <sub>3</sub> , MeOH, 90 °C, 24 h	99
5 <sup>d</sup>	<b>13b</b>	TMSN <sub>3</sub> , MeOH, 90 °C, 24 h	97
6	<b>13b</b>	TMSN <sub>3</sub> , CH <sub>3</sub> CN, 90 °C, 24 h	52
7	<b>13b</b>	TMSN <sub>3</sub> , H <sub>2</sub> O, 90 °C, 24 h	NR
8	<b>13b</b>	TMSN <sub>3</sub> , benzene, 90 °C, 24 h	31
9	<b>13b</b>	TMSN <sub>3</sub> , toluene, 90 °C, 24 h	32
10	<b>13b</b>	TMSN <sub>3</sub> , xylene, 90 °C, 24 h	39
11	<b>13b</b>	NaN <sub>3</sub> , MeOH, 90 °C, 24 h	32
12	<b>13b</b>	DIPA, MeOH, 90 °C, 24 h	87
13	<b>13c</b>	TMSN <sub>3</sub> , MeOH, 90 °C, 24 h	31 <sup>e</sup>
14	<b>13a</b>	TMSN <sub>3</sub> , neat, 100 °C, 24 h	42
15	<b>13a</b>	TMSN <sub>3</sub> , EtOH, 100 °C, 24 h	21

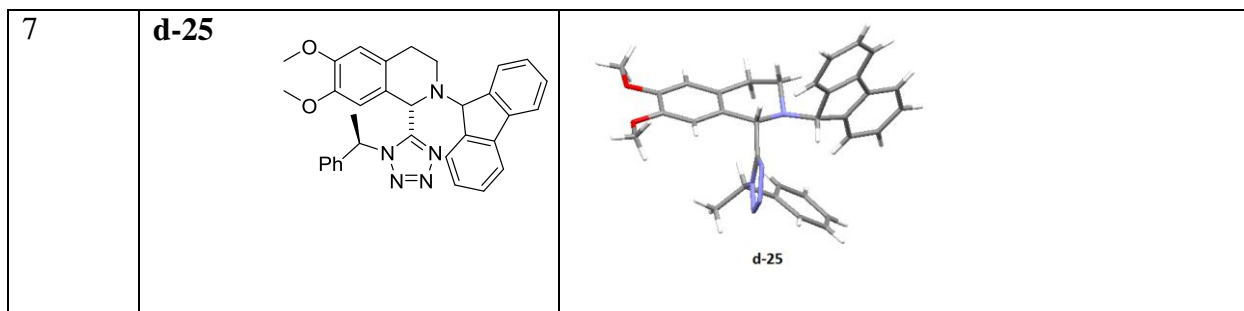
16	<b>13a</b>	TMSN <sub>3</sub> , H <sub>2</sub> O, 100 °C, 24 h	-
17	<b>13a</b>	TMSN <sub>3</sub> , MeOH:H <sub>2</sub> O (1:1), 100 °C, 24h	21
18	<b>13a</b>	NaN <sub>3</sub> , MeOH, 100 °C, 24h	trace
19	<b>13b</b>	TMSN <sub>3</sub> , EtOH, 100 °C, 24h	54
20	<b>13a</b>	TMSN <sub>3</sub> , H <sub>2</sub> O, 100 °C, 24h	-
21	<b>13b</b>	TMSN <sub>3</sub> , MeOH:H <sub>2</sub> O (1:1), 100 °C, 24h	30
22	<b>13c</b>	TMSN <sub>3</sub> , MeOH, 100 °C, 24h	-
23	<b>13d</b>	TMSN <sub>3</sub> , MeOH, 100 °C, 12h	-
24	<b>13e</b>	TMSN <sub>3</sub> , MeOH, 100 °C, 24h	-

<sup>a</sup>Reactions were performed in a closed vessel with isocyanide (0.13 mmol, 1 equiv), azide (1 equiv), **13** (1.2 equiv) and pyrrolidine [3 equiv]. <sup>b</sup>Oil bath temperature is mentioned. <sup>c</sup>isolated yields. <sup>d</sup>reaction was carried out in round bottom flask under conventional heating. <sup>e</sup> See SI for the structure of the product **13ca**, R = 2,6-dibromo fluorenyl.

**Table s2: Crystal Structures**

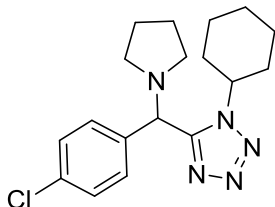


2	<b>17c</b> 	 <b>17c</b>
3	<b>17d</b> 	 <b>17d</b>
4	<b>19d</b> 	 <b>19d</b>
5	<b>d-23</b> 	 <b>d-23</b>
6	<b>24</b> 	 <b>24</b>



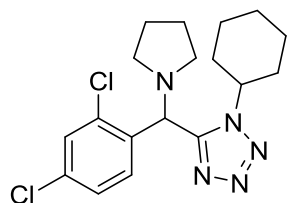
**General procedure I:** Isocyanides derivatives (0.13 mmol, 1 equiv) and trimethylsilyl azide (0.13 mmol, 1 equiv) were added to the solution of aldehydes or ketones or imine (0.15 mmol, 1.2 equiv) and *N* heterocycles (0.38 mmol, 3 equiv) in methanol (2 mL) and the mixture was stirred at 100 °C (oil bath temperature) for 10 - 24 hours. After completion of the reaction, the solvent was evaporated under reduced pressure and the residue was purified by column chromatography to obtain analytically pure  $\alpha$ - tetrazoyl *N* heterocycles.

**5-((4-chlorophenyl)(pyrrolidin-1-yl)methyl)-1-cyclohexyl-1H-tetrazole(11a):** According to



the general procedure I : *Para*-chloro benzaldehyde (0.15 mmol, 1.2 equiv, 21 mg), pyrrolidine (0.38 mmol, 3 equiv, 31  $\mu$ L), trimethylsilyl azide (0.13 mmol, 1 equiv, 17  $\mu$ L) and cyclohexyl isocyanide (0.13 mmol, 1 equiv, 16 $\mu$ L) in 2 mL methanol were reacted for 12 hours. The crude product was purified by SiO<sub>2</sub> column chromatography (ethyl acetate: hexane; 1:10) to obtain **11a** as white solid (46 mg, 95%). FTIR (KBr):  $\tilde{\nu}$  = 3423, 3096, 2935, 2861, 2789, 1564, 1586, 1468, 1262, 1093, 859, 825, 803, 749 cm<sup>-1</sup>. <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>)  $\delta$  = 7.43 (d, *J* = 8.4 Hz, 2H), 7.32 (d, *J* = 8.4 Hz, 2H), 4.96 (s, 1H), 4.63 – 4.55 (m, 1H), 2.65 – 2.60 (m, 2H), 2.43 – 2.38 (m, 2H), 2.01 – 1.92 (m, 2H), 1.84 – 1.80 (m, 5H), 1.77 – 1.70 (m, 2H), 1.47 – 1.44 (m, 1H), 1.38 – 1.22 (m, 4H). <sup>13</sup>C NMR (101 MHz, CDCl<sub>3</sub>)  $\delta$  = 154.1, 135.9, 134.4, 129.6, 129.1, 64.0, 58.2, 53.1, 33.1, 32.9, 25.7, 25.5, 25.0, 23.7 ppm. HRMS (ESI) exact mass calculated for C<sub>18</sub>H<sub>25</sub>ClN<sub>5</sub><sup>+</sup>([M+H]<sup>+</sup>): 346.1793, found: 346.1794.

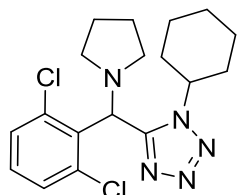
**1-cyclohexyl-5-((2,4-dichlorophenyl)(pyrrolidin-1-yl)methyl)-1H tetrazole(11b):** According



to the general procedure I : 2,4-Di-chloro benzaldehyde (0.15 mmol, 1.2 equiv, 26 mg), pyrrolidine (0.38 mmol, 3 equiv, 31  $\mu$ L), trimethylsilyl azide (0.13 mmol, 1 equiv, 17  $\mu$ L) and cyclohexyl isocyanide (0.13 mmol, 1 equiv, 16 $\mu$ L) in 2 mL methanol were reacted for 14 hours. The crude product was purified by SiO<sub>2</sub> column chromatography (ethyl acetate: hexane; 1:10) to obtain **11b** as

white solid (46 mg, 94%). FTIR (KBr):  $\tilde{\nu}$  = 3423, 3096, 3063, 1564, 1586, 1468, 1450, 1262, 1093, 825, 803 749, 695  $\text{cm}^{-1}$ . <sup>1</sup>H NMR (600 MHz, CDCl<sub>3</sub>)  $\delta$  = 7.81 (d, *J* = 8.4 Hz, 1H), 7.40 (d, *J* = 1.8 Hz, 1H), 7.31 – 7.30(m, 1H), 5.37 (s, 1H), 4.44 – 4.39 (m, 1H), 2.56 – 2.51(m, 4H), 2.02 – 1.93 (m, 2H), 1.91 – 1.87 (m, 3H), 1.86 – 1.79 (m, 4H), 1.76 – 1.74(m, 1H), 1.63 – 1.59(m, 1H), 1.46 – 1.25 (m, 3H). <sup>13</sup>C NMR (151 MHz, CDCl<sub>3</sub>)  $\delta$  = 154.8, 136.0, 134.8, 134.5, 133.2, 130.5, 129.3, 59.7, 59.2, 53.6, 34.1, 26.6, 25.9, 24.5 ppm. HRMS (ESI) exact mass calculated for C<sub>18</sub>H<sub>24</sub>Cl<sub>2</sub>N<sub>5</sub><sup>+</sup>([M+H]<sup>+</sup>): 380.1403, found: 380.1410.

**1-cyclohexyl-5-((2,6-dichlorophenyl)(pyrrolidin-1-yl)methyl)-1H-tetrazole (11c):** According



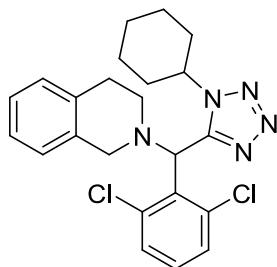
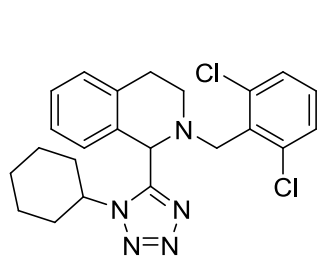
to the general procedure I : 2,6-Di-chloro benzaldehyde (0.15 mmol, 1.2 equiv, 26 mg), pyrrolidine (0.38 mmol, 3 equiv, 31  $\mu$ L), trimethylsilyl azide (0.13 mmol, 1 equiv, 17  $\mu$ L) and cyclohexyl isocyanide (0.13 mmol, 1 equiv, 16 $\mu$ L) in 2 mL methanol were reacted for 14 hours. The crude product was

purified by SiO<sub>2</sub> column chromatography (ethyl acetate: hexane; 1:10) to obtain **11c** as white solid (46 mg, 94%). FTIR (KBr):  $\tilde{\nu}$  = 3448, 3117, 3062, 2982, 2951, 2939, 2810, 1572, 1557, 1429, 1415, 1185, 1165, 880, 795, 746, 675, 425 $\text{cm}^{-1}$ . <sup>1</sup>H NMR (600 MHz, CDCl<sub>3</sub>)  $\delta$  = 7.39 – 7.37 (m, 2H), 7.28 – 7.27 (m, 1H), 5.83 (s, 1H), 3.84 – 3.79 (m, 1H), 3.01 – 2.98 (m, 2H), 2.74 – 2.71 (m, 2H), 2.01 – 1.97 (m, 2H), 1.92 – 1.83 (m, 4H), 1.77 – 1.73 (m, 2H), 1.69 – 1.62 (m, 2H), 1.32 – 1.20 (m, 2H), 1.14 – 1.10 (m, 1H), 0.92 – 0.84 (m, 1H). <sup>13</sup>C NMR (151 MHz, CDCl<sub>3</sub>)  $\delta$  = 153.4, 136.7, 132.2, 130.6, 129.9, 59.5, 58.2, 52.1, 33.1, 32.6, 25.7, 25.5, 24.9, 23.7 ppm. HRMS (ESI) exact mass calculated for C<sub>18</sub>H<sub>24</sub>Cl<sub>2</sub>N<sub>5</sub><sup>+</sup>([M+H]<sup>+</sup>): 380.1403, found: 380.1393

**2-((1-cyclohexyl-1H-tetrazol-5-yl)(2,6-dichlorophenyl)methyl)-**

**1,2,3,4-tetrahydroisoquinoline and 1-(1-cyclohexyl-1H-tetrazol-5-yl)-2-(2,6-dichlorobenzyl)-**

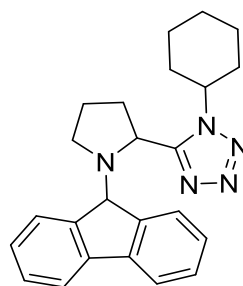
**1,2,3,4-tetrahydroisoquinoline(12a and 12b):** According to the general procedure I : 2,6-Di-



chloro benzaldehyde (0.15 mmol, 1.2 equiv, 26 mg), 1,2,3,4-tetrahydroisoquinoline (0.38 mmol, 3 equiv, 48  $\mu$ L), trimethylsilyl azide (0.13 mmol, 1 equiv, 17  $\mu$ L) and cyclohexyl isocyanide (0.13 mmol, 1 equiv, 17  $\mu$ L) in 2

mL methanol were reacted for 14 hours. The crude product was purified by SiO<sub>2</sub> column chromatography (ethyl acetate: hexane; 1:6) to obtain an inseparable mixture of **12a and 12b** as white solid (57 mg, 99%). ppm. Characteristic signals of both the isomer are mentioned <sup>1</sup>H NMR (600 MHz, CDCl<sub>3</sub>)  $\delta$  = 5.98 (s, 1.4H), 5.44 (s, 1H), 4.15 (d,  $J$  = 15.0 Hz, 1H), 4.09 – 4.08 (m, 1H), 4.06 (d,  $J$  = 9.1 Hz, 1H), 3.94 (d,  $J$  = 12.6 Hz, 1H). <sup>13</sup>C NMR (151 MHz, CDCl<sub>3</sub>)  $\delta$  = 155.1, 152.9, 137.3, 136.9, 135.0, 134.6, 134.3, 133.5, 132.3, 131.6, 130.8, 130.1, 129.6, 129.1, 128.8, 128.7, 128.2, 127.8, 126.9, 126.7, 126.2, 125.7, 61.1, 58.9, 58.4, 58.1, 54.2, 52.8, 48.5, 47.6, 33.2, 32.6, 32.4, 29.7, 28.3, 25.7, 25.6, 25.50, 25.46, 25.0, 24.9 ppm. HRMS (ESI) exact mass calculated for C<sub>23</sub>H<sub>26</sub>Cl<sub>2</sub>N<sub>5</sub><sup>+</sup> ([M+H]<sup>+</sup>): 442.1560, found: 442.1549.

**5-(1-(9H-fluoren-9-yl)pyrrolidin-2-yl)-1-cyclohexyl-1H-tetrazole (14a):** According to the

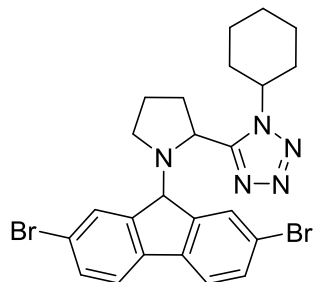


general procedure I : 9-fluorenone imine (0.15 mmol, 1.2 equiv, 27 mg), pyrrolidine (0.38 mmol, 3 equiv, 31  $\mu$ L), trimethylsilyl azide (0.13 mmol, 1 equiv, 17  $\mu$ L) and cyclohexyl isocyanide (0.13 mmol, 1 equiv, 16  $\mu$ L) in 2 mL methanol were reacted for 24 hours. The crude product was purified by SiO<sub>2</sub> column chromatography (ethyl acetate: hexane; 1:5) to obtain **13a** as light yellow solid (50 mg, 99.9%). FTIR (KBr):  $\tilde{\nu}$  = 3064, 2947, 2853, 2807,

1450, 1442, 1302, 1263, 1181, 1158, 1137, 1101, 1075, 1006, 899, 789, 747, 676, 620 cm<sup>-1</sup>. <sup>1</sup>H NMR (600 MHz, CDCl<sub>3</sub>)  $\delta$  = 7.68 (d,  $J$  = 7.8 Hz, 1H), 7.65 (t,  $J$  = 7.8 Hz, 2H), 7.51 (d,  $J$  = 7.2 Hz, 1H), 7.39 (t,  $J$  = 7.2 Hz, 1H), 7.34 – 7.30 (m, 2H), 7.22 – 7.19 (m, 1H), 4.75 (s, 1H), 4.70 (t,  $J$  = 7.8 Hz, 1H), 4.60 – 4.55 (m, 1H), 2.93 – 2.89 (m, 1H), 2.47 – 2.43 (m, 1H), 2.28 – 2.22 (m, 1H), 2.06 – 1.98 (m, 6H), 1.94 – 1.90 (m, 1H), 1.84 – 1.83 (m, 1H), 1.81 – 1.78 (m, 2H), 1.49 – 1.44 (m, 1H), 1.39 – 1.33 (m, 2H). <sup>13</sup>C NMR (151 MHz, CDCl<sub>3</sub>)  $\delta$  = 155.1, 144.3, 142.2, 141.1, 140.9, 128.64, 128.61, 127.6, 127.4, 127.0, 125.1, 120.1, 119.9, 64.1, 58.0, 54.7, 48.0, 33.8, 33.1, 32.0,

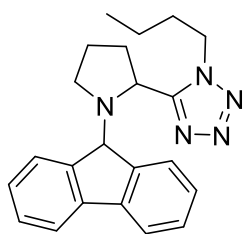
25.6, 25.1, 23.1 ppm. HRMS (ESI) exact mass calculated for  $C_{24}H_{28}N_5^+$  ( $[M+H]^+$ ): 386.2339, found: 386.2336.

**1-cyclohexyl-5-(1-(2,7-dibromo-9H-fluoren-9-yl)pyrrolidin-2-yl)-1H-tetrazole (13ca):**



According to the general procedure: 2,7 di-bromo 9-fluorenone (0.15 mmol, 1.2 equiv, 50 mg), pyrrolidine (0.38 mmol, 3 equiv, 31  $\mu$ L), trimethylsilyl azide (0.13 mmol, 1 equiv, 17  $\mu$ L) and cyclohexyl isocyanide (0.13 mmol, 1 equiv, 16  $\mu$ L) in 2 mL methanol were reacted for 36 hours. The crude product was purified by  $SiO_2$  column chromatography (ethyl acetate: hexane; 1:4) to obtain **13ca** as light yellow solid (22 mg, 31%). FTIR (KBr):  $\tilde{\nu}$  = 3448, 2853, 1560, 1450, 1442, 1263, 1158, 899, 789, 676  $cm^{-1}$ .  $^1H$  NMR (600 MHz,  $CDCl_3$ )  $\delta$  = 7.81 (s, 1H), 7.59 (s, 1H), 7.51 – 7.50 (m, 4H), 4.86 – 4.83 (m, 2H), 4.77 – 4.73 (m, 1H), 4.68 (s, 1H), 2.78 – 2.77 (m, 1H), 2.39 – 2.28 (m, 2H), 2.23 – 2.17 (m, 1H), 2.11 – 1.93 (m, 8H), 1.85 – 1.84 (m, 2H), 1.59 – 1.55 (m, 1H), 1.47 – 1.39 (m, 2H).  $^{13}C$  NMR (151 MHz,  $CDCl_3$ )  $\delta$  = 154.4, 146.2, 144.1, 139.4, 138.6, 132.1, 132.0, 129.9, 128.4, 122.0, 121.8, 121.49, 121.48, 63.6, 58.4, 55.6, 47.2, 33.8, 33.6, 31.6, 25.8, 25.7, 25.1, 23.0. HRMS (ESI) exact mass calculated for  $C_{24}H_{26}Br_2N_5^+$  ( $[M+H]^+$ ): 542.0549, found: 542.0550.

**5-(1-(9H-fluoren-9-yl)pyrrolidin-2-yl)-1-butyl-1H-tetrazole(14b):**

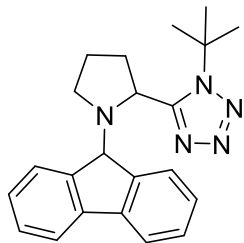


According to the general procedure I: 9-fluorenone imine (0.15 mmol, 1.2 equiv, 27 mg), pyrrolidine (0.38 mmol, 3 equiv, 31  $\mu$ L), trimethylsilyl azide (0.13 mmol, 1 equiv, 17  $\mu$ L) and *n*-butyl isocyanide (0.13 mmol, 1 equiv, 16  $\mu$ L) in 2 mL methanol were reacted for 20 hours. The crude product was purified by  $SiO_2$  column chromatography (ethyl acetate: hexane; 1:3) to obtain **14b** as white solid (33 mg, 70%). FTIR (KBr):  $\tilde{\nu}$  = 2958, 2871, 1966, 1438, 1301, 1200, 1159, 946, 830, 748, 677  $cm^{-1}$ .  $^1H$  NMR (600 MHz,  $CDCl_3$ )  $\delta$  = 7.69 (d,  $J$  = 7.8 Hz, 1H), 7.64 (d,  $J$  = 7.2 Hz, 1H), 7.56 (d,  $J$  = 7.2 Hz, 1H), 7.50 (d,  $J$  = 7.2 Hz, 1H), 7.41 – 7.39 (m, 1H), 7.32 – 7.30 (m, 2H), 7.17 – 7.14 (m, 1H), 4.85 (s, 1H), 4.51 – 4.48 (m, 1H), 4.33 – 4.28 (m, 1H), 4.10 – 4.05 (m, 1H), 3.12 – 3.08 (m, 1H), 2.76 – 2.72 (m, 1H), 2.26 – 2.20 (m, 1H), 2.10 – 2.05 (m, 1H), 1.95 – 1.92 (m, 1H), 1.88 – 1.85 (m, 1H), 1.83 – 1.78 (m, 2H), 1.37 – 1.34 (m, 2H), 0.94 (t,  $J$  = 7.4 Hz, 3H).  $^{13}C$  NMR (151 MHz,  $CDCl_3$ )  $\delta$  = 156.4, 144.1, 142.6, 141.1, 140.9, 128.7, 128.6, 127.6, 127.4, 126.6, 125.5, 120.1,



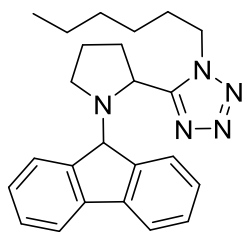
119.9, 64.5, 53.8, 49.3, 47.2, 32.2, 32.0, 23.7, 20.1, 13.7 ppm. HRMS (ESI) exact mass calculated for  $C_{22}H_{26}N_5^+$  ( $[M+H]^+$ ): 360.2183, found: 360.2182.

**5-(1-(9H-fluoren-9-yl)pyrrolidin-2-yl)-1-(tert-butyl)-1H-tetrazole(14c)** : According to the



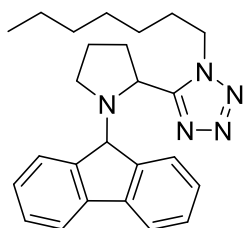
general procedure I: 9-fluorenone imine (0.15 mmol, 1.2 equiv, 27 mg), pyrrolidine (0.38 mmol, 3 equiv, 31  $\mu$ L), trimethylsilyl azide (0.13 mmol, 1 equiv, 17  $\mu$ L) and *tert*-butyl isocyanide (0.13 mmol, 1 equiv, 16  $\mu$ L) in 2 mL methanol were reacted for 20 hours. The crude product was purified by  $SiO_2$  column chromatography (ethyl acetate: hexane; 1:3) to obtain **14c** as light yellow solid (40 mg, 86%). FTIR (KBr):  $\tilde{\nu}$  =  $^1H$  NMR (600 MHz,  $CDCl_3$ )  $\delta$  = 7.81 (d,  $J$  = 7.8 Hz, 1H), 7.68 (d,  $J$  = 7.2 Hz, 1H), 7.58 (d,  $J$  = 7.8 Hz, 1H), 7.40 (t,  $J$  = 7.2 Hz, 1H), 7.36 (d,  $J$  = 7.8 Hz, 1H), 7.33 – 7.30 (m, 1H), 7.23 – 7.21 (t,  $J$  = 7.4 Hz, 1H), 7.10 – 7.03 (m, 1H), 5.14 (s, 1H), 4.24 – 4.22 (m, 1H), 3.63 – 3.61 (m, 1H), 3.43 – 3.38 (m, 1H), 2.34 – 2.28 (m, 1H), 2.15 – 2.11 (m, 1H), 1.96 – 1.93 (m, 1H), 1.73 – 1.7 (m, 1H), 1.29 (s, 9H).  $^{13}C$  NMR (151 MHz,  $CDCl_3$ )  $\delta$  = 159.7, 144.7, 143.8, 141.2, 140.4, 128.6, 128.3, 127.5, 127.2, 126.7, 126.2, 119.9, 119.7, 65.6, 60.4, 54.2, 52.0, 34.6, 29.8, 24.3 ppm. HRMS (ESI) exact mass calculated for  $C_{22}H_{26}N_5^+$  ( $[M+H]^+$ ): 360.2183, found: 360.2175.

**5-(1-(9H-fluoren-9-yl)pyrrolidin-2-yl)-1-hexyl-1H-tetrazole(14d)**: According to the general



procedure I: 9-fluorenone imine (0.15 mmol, 1.2 equiv, 27 mg), pyrrolidine (0.38 mmol, 3 equiv, 31  $\mu$ L), trimethylsilyl azide (0.13 mmol, 1 equiv, 17  $\mu$ L) and *n*-hexyl isocyanide (0.13 mmol, 1 equiv, 14 mg) in 2 mL methanol were reacted for 14 hours. The crude product was purified by  $SiO_2$  column chromatography (ethyl acetate: hexane; 1:4) to obtain **14d** as brown solid (27 mg, 64 %).  $^1H$  NMR (600 MHz,  $CDCl_3$ )  $\delta$  = 7.70 (d,  $J$  = 7.8 Hz, 1H), 7.65 (d,  $J$  = 7.2 Hz, 1H), 7.57 (d,  $J$  = 7.2 Hz, 1H), 7.50 (d,  $J$  = 7.2 Hz, 1H), 7.42 – 7.39 (m, 1H), 7.33 – 7.30 (m, 2H), 7.17 – 7.14 (m, 1H), 4.86 (s, 1H), 4.51 – 4.49 (m, 1H), 4.31 – 4.27 (m, 1H), 4.09 – 4.04 (m, 1H), 3.13 – 3.08 (m, 1H), 2.77 – 2.72 (m, 1H), 2.26 – 2.22 (m, 1H), 2.12 – 2.04 (m, 1H), 1.95 – 1.91 (m, 1H), 1.89 – 1.82 (m, 3H), 1.33 – 1.28 (m, 6H), 0.89 (t,  $J$  = 7.2 Hz, 3H).  $^{13}C$  NMR (151 MHz,  $CDCl_3$ )  $\delta$  = 156.4, 144.1, 142.6, 141.1, 140.9, 128.7, 128.6, 127.6, 127.4, 126.6, 125.6, 120.1, 119.9, 64.5, 53.8, 49.3, 47.5, 32.2, 31.3, 30.0, 26.5, 23.7, 22.6, 14.2. HRMS (ESI) exact mass calculated for  $C_{24}H_{30}N_5^+$  ( $[M+H]^+$ ): 388.2496, found: 388.2500.

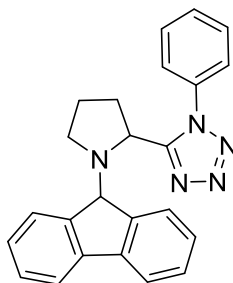
**5-(1-(9H-fluoren-9-yl)pyrrolidin-2-yl)-1-heptyl-1H-tetrazole (14e):** According to the general



procedure I: 9-fluorenone imine (0.15 mmol, 1.2 equiv, 27 mg), pyrrolidine (0.38 mmol, 3 equiv, 31  $\mu$ L), trimethylsilyl azide (0.13 mmol, 1 equiv, 17  $\mu$ L) and *n*-heptyl isocyanide (0.13 mmol, 1 equiv, 16 mg) in 2 mL methanol were reacted for 14 hours. The crude product was purified by SiO<sub>2</sub> column chromatography (ethyl acetate: hexane; 1:4) to obtain **14e** as brown solid.

(34 mg, 64 %) FTIR (KBr):  $\tilde{\nu}$  = 3065, 2951, 2927, 2860, 1449, 1301, 736, 673, 621 cm<sup>-1</sup>. <sup>1</sup>H NMR (600 MHz, CDCl<sub>3</sub>)  $\delta$  = 7.69 (d, *J* = 7.8 Hz, 1H), 7.64 (d, *J* = 7.8 Hz, 1H), 7.56 (d, *J* = 7.8 Hz, 1H), 7.50 (d, *J* = 7.2 Hz, 1H), 7.41 – 7.39 (m, 1H), 7.32 – 7.30 (m, 2H), 7.17 – 7.14 (m, 1H), 4.84 (s, 1H), 4.52 – 4.49 (m, 1H), 4.32 – 4.27 (m, 1H), 4.10 – 4.05 (m, 1H), 3.12 – 3.07 (m, 1H), 2.75 – 2.71 (m, 1H), 2.26 – 2.20 (m, 1H), 2.10 – 2.04 (m, 1H), 1.95 – 1.91 (m, 1H), 1.87 – 1.81 (m, 3H), 1.34 – 1.25 (m, 8H), 0.88 (t, *J* = 7.2 Hz, 3H). <sup>13</sup>C NMR (101 MHz, CDCl<sub>3</sub>)  $\delta$  = 156.3, 144.1, 142.6, 141.0, 140.9, 128.7, 128.6, 127.5, 127.4, 126.5, 125.5, 120.1, 119.9, 64.5, 53.9, 49.2, 47.5, 32.1, 31.7, 30.0, 28.8, 26.8, 23.7, 22.7, 14.2 ppm. HRMS (ESI) exact mass calculated for C<sub>25</sub>H<sub>32</sub>N<sub>5</sub><sup>+</sup> ([M+H]<sup>+</sup>): 402.2652, found: 402.2646.

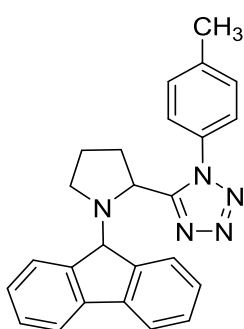
**5-(1-(9H-fluoren-9-yl)pyrrolidin-2-yl)-1-phenyl-1H-tetrazole(14f):** According to the general



procedure I: 9-fluorenone imine (0.15 mmol, 1.2 equiv, 27 mg), pyrrolidine (0.38 mmol, 3 equiv, 31  $\mu$ L), trimethylsilyl azide (0.13 mmol, 1 equiv, 17  $\mu$ L) and phenyl isocyanide (0.13 mmol, 1 equiv, 17 mg) in 2 mL methanol were reacted for 14 hours 16 hours. The crude product was purified by SiO<sub>2</sub> column chromatography (ethyl acetate: hexane; 1:5) to obtain **14f** as brown solid (32 mg, 64 %). FTIR (KBr):  $\tilde{\nu}$  = <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>)  $\delta$  = 7.58 – 7.53 (m,

2H), 7.50 – 7.42 (m, 4H), 7.34 – 7.27 (m, 3H), 7.23 – 7.19 (m, 3H), 7.12 – 7.08 (m, 1H), 4.94 (s, 1H), 4.35 – 4.32 (m, 1H), 3.23 – 3.17 (m, 1H), 2.89 – 2.83 (m, 1H), 2.14 – 2.03 (m, 2H), 1.99 – 1.95 (m, 1H), 1.84 – 1.82 (m, 1H). <sup>13</sup>C NMR (101 MHz, CDCl<sub>3</sub>)  $\delta$  = 158.2, 144.1, 143.2, 140.85, 140.82, 134.0, 130.4, 129.6, 128.45, 128.43, 127.4, 127.2, 126.3, 125.7, 125.6, 119.9, 119.8, 64.9, 53.2, 50.2, 32.5, 24.1 (one aromatic carbon is merging in aromatic region) ppm. HRMS (ESI) exact mass calculated for C<sub>24</sub>H<sub>22</sub>N<sub>5</sub><sup>+</sup> ([M+H]<sup>+</sup>): 380.1870, found: 380.1859.

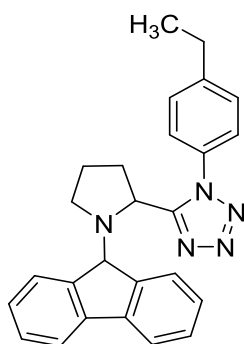
**5-(1-(9H-fluoren-9-yl)pyrrolidin-2-yl)-1-(p-tolyl)-1H-tetrazole(14g):** According to the general



procedure I: 9-fluorenone imine (0.15 mmol, 1.2 equiv, 27 mg), pyrrolidine (0.38 mmol, 3 equiv, 31  $\mu$ L), trimethylsilyl azide (0.13 mmol, 1 equiv, 17  $\mu$ L) and *para*-methyl phenyl isocyanide (0.13 mmol, 1 equiv, 15 mg) in 2 mL methanol were reacted for 12 hours. The crude product was purified by SiO<sub>2</sub> column chromatography (ethyl acetate: hexane; 1:5) to obtain **14g** as brown solid (35 mg, 69 %). FTIR (KBr):  $\tilde{\nu}$  = 2924, 2853, 1644, 1516, 1448, 1384, 1124, 1098, 822, 745, 669 cm<sup>-1</sup>. . <sup>1</sup>H NMR (600 MHz, CDCl<sub>3</sub>)  $\delta$  =

7.59 (d,  $J$  = 7.2 Hz, 1H), 7.55 (d,  $J$  = 7.2 Hz, 1H), 7.49 (d,  $J$  = 7.2 Hz, 1H), 7.33 – 7.28 (m, 3H), 7.24 – 7.21 (m, 3H), 7.11 – 7.07 (m, 3H), 4.93 (s, 1H), 4.36 – 4.34 (m, 1H), 3.16 – 3.13 (m, 1H), 2.83 – 2.79 (m, 1H), 2.43 (s, 3H), 2.12 – 2.02 (m, 2H), 1.97 – 1.93 (m, 1H), 1.82 – 1.77 (m, 1H). <sup>13</sup>C NMR (151 MHz, CDCl<sub>3</sub>)  $\delta$  = 158.1, 144.2, 143.2, 140.9, 140.8, 140.7, 131.5, 130.1, 128.4, 128.3, 127.4, 127.2, 126.4, 125.7, 125.4, 119.9, 119.8, 64.8, 53.4, 49.9, 32.4, 24.1, 21.4. HRMS (ESI) exact mass calculated for C<sub>25</sub>H<sub>24</sub>N<sub>5</sub><sup>+</sup> ([M+H]<sup>+</sup>): 394.2026, found: 394.2027.

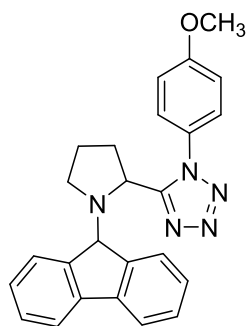
**5-(1-(9H-fluoren-9-yl)pyrrolidin-2-yl)-1-(4-ethylphenyl)-1H-tetrazole (14h):** According to



the general procedure I: 9-fluorenone imine (0.15 mmol, 1.2 equiv, 27 mg), pyrrolidine (0.38 mmol, 3 equiv, 31  $\mu$ L), trimethylsilyl azide (0.13 mmol, 1 equiv, 17  $\mu$ L) and *para*-ethyl phenyl isocyanide (0.13 mmol, 1 equiv, 17 mg) in 2 mL methanol were reacted for 12 hours. The crude product was purified by SiO<sub>2</sub> column chromatography (ethyl acetate: hexane; 1:5) to obtain **14h** as brown solid (36 mg, 68 %). FTIR (KBr):  $\tilde{\nu}$  = 3036, 2963, 2848, 1959, 1518, 1448, 1369, 1320, 1237, 1151, 1100, 1073, 841, 746, 729, 612, 565

cm<sup>-1</sup>. <sup>1</sup>H NMR (600 MHz, CDCl<sub>3</sub>)  $\delta$  = 7.57 (d,  $J$  = 7.8 Hz, 1H), 7.53 (d,  $J$  = 7.8 Hz, 1H), 7.46 (d,  $J$  = 7.8 Hz, 1H), 7.31 – 7.29 (m, 3H), 7.25 (d,  $J$  = 7.8 Hz, 2H), 7.21 (t,  $J$  = 7.2 Hz, 1H), 7.11 – 7.08 (m, 3H), 4.91 (s, 1H), 4.37 – 4.35 (m, 1H), 3.16 – 3.13 (m, 1H), 2.82 – 2.78 (m, 1H), 2.74 – 2.70 (m, 2H), 2.15 – 2.01 (m, 2H), 2.00 – 1.96 (m, 1H), 1.83 – 1.79 (m, 1H), 1.29 (t,  $J$  = 7.8 Hz, 3H). <sup>13</sup>C NMR (151 MHz, CDCl<sub>3</sub>)  $\delta$  = 158.0, 146.9, 144.3, 143.2, 140.9, 140.8, 131.7, 128.9, 128.4, 127.4, 127.2, 126.4, 125.7, 125.5, 119.9, 119.8, 64.8, 53.4, 49.8, 32.5, 28.8, 24.0, 15.6 ppm. (Total count of <sup>13</sup>C is less than expected due to the merging of signals in the aromatic region). HRMS (ESI) exact mass calculated for C<sub>26</sub>H<sub>26</sub>N<sub>5</sub><sup>+</sup> ([M+H]<sup>+</sup>): 408.2183, found: 408.2184.

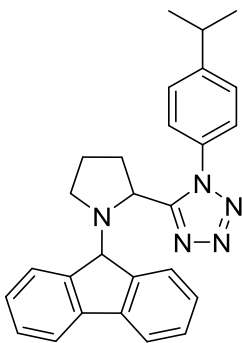
**5-(1-(9H-fluoren-9-yl)pyrrolidin-2-yl)-1-(4-methoxyphenyl)-1H-tetrazole (14i):** According to



the general procedure I: 9-fluorenone imine (0.15 mmol, 1.2 equiv, 27 mg), pyrrolidine (0.38 mmol, 3 equiv, 31  $\mu$ L), trimethylsilyl azide (0.13 mmol, 1 equiv, 17  $\mu$ L) and *para*-methoxy phenyl isocyanide (0.13 mmol, 1 equiv, 17 mg) in 2 mL methanol were reacted for 16 hours. The crude product was purified by SiO<sub>2</sub> column chromatography (ethyl acetate: hexane; 1:5) gave **14i** as light yellow solid (42 mg, 82 %). FTIR (KBr):  $\tilde{\nu}$  = 3401, 2924, 2853,

1609, 1444, 1256, 1023, 823, 743 cm<sup>-1</sup>. <sup>1</sup>H NMR (600 MHz, CDCl<sub>3</sub>)  $\delta$  = 7.53 (d, *J* = 7.8 Hz, 1H), 7.50 (d, *J* = 7.5 Hz, 1H), 7.45 (d, *J* = 7.8 Hz, 1H), 7.28 – 7.26 (m, 1H), 7.25 – 7.22 (d, *J* = 8.1 Hz, 2H), 7.18 – 7.16 (m, 1H), 7.06 – 7.03 (m, 3H), 6.86 – 6.85 (m, 2H), 4.88 (s, 1H), 4.27 – 4.25 (m, 1H), 3.80 (s, 3H), 3.11 – 3.08 (m, 1H), 2.78 – 2.74 (m, 1H), 2.05 – 1.94 (m, 2H), 1.90 – 1.86 (m, 1H), 1.76 – 1.71 (m, 1H). <sup>13</sup>C NMR (151 MHz, CDCl<sub>3</sub>)  $\delta$  = 160.9, 158.2, 144.2, 143.2, 140.9, 140.8, 128.4, 127.5, 127.2, 127.0, 126.7, 126.4, 125.8, 119.9, 119.8, 114.6, 6.83, 55.9, 53.3, 49.9, 32.3, 24.1. HRMS (ESI) exact mass calculated for C<sub>25</sub>H<sub>24</sub>N<sub>5</sub>O<sup>+</sup> ([M+H]<sup>+</sup>): 410.1975, found: 410.1978.

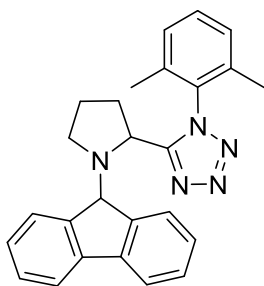
**5-(1-(9H-fluoren-9-yl)pyrrolidin-2-yl)-1-(4-isopropylphenyl)-1H-tetrazole(14j):** According to



the general procedure: 9-fluorenone imine (0.15 mmol, 1.2 equiv, 27 mg), pyrrolidine (0.38 mmol, 3 equiv, 31  $\mu$ L), trimethylsilyl azide (0.13 mmol, 1 equiv, 17  $\mu$ L) and *para*-isopropyl phenyl isocyanide (0.13 mmol, 1 equiv, 19 mg) in 2 mL methanol were reacted for 16 hours. The crude product was purified by SiO<sub>2</sub> column chromatography (ethyl acetate: hexane; 1:4) to obtain **14j** as brown solid (33 mg, 60 %). FTIR (KBr):  $\tilde{\nu}$  = 3061, 3035, 2961, 2926, 2847, 1956, 1913, 1585, 1514, 1445, 1364, 1206,

1128, 1099, 840, 746, 668, 574 cm<sup>-1</sup>. <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>)  $\delta$  = 7.57 (d, *J* = 7.6 Hz, 1H), 7.52 (d, *J* = 7.6 Hz, 1H), 7.44 (d, *J* = 7.2 Hz, 1H), 7.31 – 7.27 (m, 5H), 7.21 (t, *J* = 7.6 Hz, 1H), 7.10 – 7.07 (m, 3H), 4.91 (s, 1H), 4.33 – 4.29 (m, 1H), 3.20 – 3.16 (m, 1H), 3.02 – 2.95 (m, 1H), 2.87 – 2.80 (m, 1H), 2.17 – 2.05 (m, 2H), 2.03 – 1.98 (m, 1H), 1.86 – 1.81 (m, 1H), 1.30 (d, *J* = 6.8 Hz, 6H). <sup>13</sup>C NMR (151 MHz, CDCl<sub>3</sub>)  $\delta$  = 158.1, 151.5, 144.2, 143.1, 140.83, 140.78, 131.6, 128.4, 127.5, 127.4, 127.2, 126.3, 125.7, 125.5, 119.9, 119.7, 64.7, 53.2, 50.0, 34.2, 32.6, 24.1, 24.1, 24.0 ppm. (Total count of <sup>13</sup>C is less than expected due to the merging of signals in the aromatic region). HRMS (ESI) exact mass calculated for C<sub>27</sub>H<sub>28</sub>N<sub>5</sub><sup>+</sup> ([M+H]<sup>+</sup>): 422.2339, found: 422.2340.

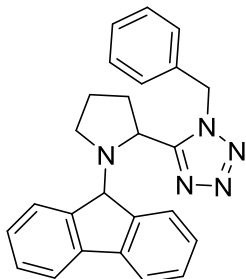
**5-(1-(9H-fluoren-9-yl)pyrrolidin-2-yl)-1-(2,6-dimethylphenyl)-1H-tetrazole (14k):** According



to the general procedure I: 9-fluorenone imine (0.15 mmol, 1.2 equiv, 27 mg), pyrrolidine (0.38 mmol, 3 equiv, 31  $\mu$ L), trimethylsilyl azide (0.13 mmol, 1 equiv, 17  $\mu$ L) and 2,6 di-methyl phenyl isocyanide (0.13 mmol, 1 equiv, 17 mg) in 2 mL methanol were reacted for 16 hours. The crude product was purified by SiO<sub>2</sub> column chromatography (ethyl acetate: hexane; 1:5) to obtain **14k** as white solid (30 mg, 57 %). FTIR (KBr):  $\tilde{\nu}$  =

3069, 2918, 2815, 1471, 1449, 1100, 748, 622  $\text{cm}^{-1}$ . <sup>1</sup>H NMR (600 MHz, CDCl<sub>3</sub>)  $\delta$  = 7.68 – 7.66 (m, 2H), 7.63 (d, *J* = 7.8 Hz, 1H), 7.40 (t, *J* = 7.8 Hz, 1H), 7.36 – 7.32 (m, 2H), 7.31 – 7.29 (m, 1H), 7.28 – 7.27 (m, 1H), 7.21 (d, *J* = 7.2 Hz, 1H), 7.16 – 7.14 (m, 1H), 7.12 – 7.1 (m, 1H), 4.80 (s, 1H), 4.54 – 4.51 (m, 1H), 2.72 – 2.69 (m, 1H), 2.22 – 2.18 (m, 1H), 2.14 – 2.09 (m, 2H), 2.05 (s, 3H), 1.99 – 1.92 (m, 1H), 1.88 (s, 3H), 1.66 – 1.62 (m, 1H). <sup>13</sup>C NMR (151 MHz, CDCl<sub>3</sub>)  $\delta$  = 159.0, 144.8, 143.5, 141.9, 139.9, 136.1, 136.0, 132.4, 131.2, 129.2, 129.1, 128.5, 128.4, 127.8, 126.9, 126.1, 125.7, 120.3, 119.6, 64.7, 55.6, 46.8, 32.2, 23.9, 17.9, 17.7. HRMS (ESI) exact mass calculated for C<sub>26</sub>H<sub>26</sub>N<sub>5</sub><sup>+</sup> ([M+H]<sup>+</sup>): 408.2183, found: 408.2184.

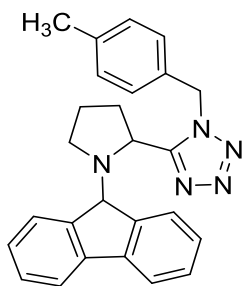
**5-(1-(9H-fluoren-9-yl)pyrrolidin-2-yl)-1-benzyl-1H-tetrazole (14l):** According to general



procedure I: 9-fluorenone imine (0.15 mmol, 1.2 equiv, 27 mg), pyrrolidine (0.38 mmol, 3 equiv, 31  $\mu$ L), trimethylsilyl azide (0.13 mmol, 1 equiv, 17  $\mu$ L) and benzyl isocyanide (0.13 mmol, 1 equiv, 15 mg) in 2 mL methanol heating at methanol were reacted for 20 hours. The crude product was purified by SiO<sub>2</sub> column chromatography (ethyl acetate: hexane; 1:5) to obtain **14l** as brown solid (37 mg, 73 %). FTIR (KBr):  $\tilde{\nu}$  = 3399, 2959, 2925,

1654, 1406, 1248, 1181, 747, 620  $\text{cm}^{-1}$ . <sup>1</sup>H NMR (600 MHz, CDCl<sub>3</sub>)  $\delta$  = 7.73 (d, *J* = 7.2 Hz, 1H), 7.67 (d, *J* = 7.8 Hz, 1H), 7.53 (d, *J* = 7.2 Hz, 1H), 7.44 – 7.41 (m, 2H), 7.32 – 7.30 (m, 2H), 7.29 – 7.27 (m, 3H), 7.16 – 7.13 (m, 1H), 7.00 – 6.99 (m, 2H), 5.71 (d, *J* = 15.0 Hz, 1H), 5.11 (d, *J* = 15.0 Hz, 1H), 4.89 (s, 1H), 4.41 – 4.36 (m, 1H), 3.15 – 3.12 (m, 1H), 2.79 – 2.75 (m, 1H), 1.99 – 1.89 (m, 2H), 1.76 – 1.72 (m, 1H), 1.64 – 1.58 (m, 1H). <sup>13</sup>C NMR (151 MHz, CDCl<sub>3</sub>)  $\delta$  = 157.0, 144.1, 142.7, 141.1, 140.8, 134.4, 129.2, 128.8, 128.7, 128.6, 127.6, 127.5, 127.3, 126.5, 125.7, 120.2, 119.9, 64.7, 53.6, 50.8, 49.8, 31.8, 23.7. HRMS (ESI) exact mass calculated for C<sub>25</sub>H<sub>24</sub>N<sub>5</sub><sup>+</sup> ([M+H]<sup>+</sup>): 394.2026, found: 394.2019.

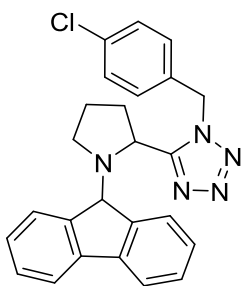
**5-(1-(9H-fluoren-9-yl)pyrrolidin-2-yl)-1-(4-methylbenzyl)-1H-tetrazole (14m):** According to



general procedure I: 9-fluorenone imine (0.15 mmol, 1.2 equiv, 27 mg), pyrrolidine (0.38 mmol, 3 equiv, 31  $\mu$ L), trimethylsilyl azide (0.13 mmol, 1 equiv, 17  $\mu$ L) and *para*-methyl benzyl isocyanide (0.13 mmol, 1 equiv, 17 mg) in 2 mL methanol were reacted for 16 hours. The crude product was purified by SiO<sub>2</sub> column chromatography (ethyl acetate: hexane; 1:5) to obtain **14m** as brown solid (43 mg, 82 %). FTIR (KBr):  $\tilde{\nu}$  = 3064, 2924,

2854, 1730, 1654, 1447, 1299, 1249, 1182, 1022, 813, 734, 673, 620, 475 cm<sup>-1</sup>. <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>)  $\delta$  = 7.72 (d,  $J$  = 7.6 Hz, 1H), 7.66 (d,  $J$  = 7.6 Hz, 1H), 7.54 (d,  $J$  = 7.6 Hz, 1H), 7.44 – 7.40 (m, 2H), 7.33 – 7.30 (m, 2H), 7.15 – 7.12 (m, 1H), 7.08 (d,  $J$  = 8.0 Hz, 2H), 6.89 (d,  $J$  = 8.0 Hz, 2H), 5.64 (d,  $J$  = 15.6 Hz, 1H), 5.08 (d,  $J$  = 15.6 Hz, 1H), 4.89 (s, 1H), 4.41 – 4.37 (m, 1H), 3.15 – 3.10 (m, 1H), 2.79 – 2.72 (m, 1H), 2.29 (s, 3H), 2.01 – 1.87 (m, 2H), 1.77 – 1.71 (m, 1H), 1.66 – 1.59 (m, 1H). <sup>13</sup>C NMR (101 MHz, CDCl<sub>3</sub>)  $\delta$  = 156.9, 144.1, 142.7, 141.1, 140.8, 138.6, 131.3, 129.8, 128.7, 128.6, 127.6, 127.4, 127.3, 126.5, 125.7, 120.1, 119.9, 64.6, 53.7, 50.6, 49.7, 31.8, 23.6, 21.3 ppm. HRMS (ESI) exact mass calculated for C<sub>26</sub>H<sub>26</sub>N<sub>5</sub><sup>+</sup> ([M+H]<sup>+</sup>): 408.2183, found: 408.2180.

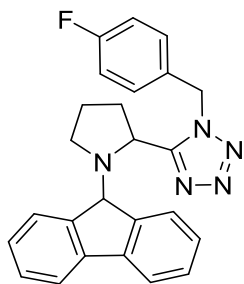
**5-(1-(9H-fluoren-9-yl)pyrrolidin-2-yl)-1-(4-chlorobenzyl)-1H-tetrazole (14n):** According to



the general procedure I: 9-fluorenone imine (0.15 mmol, 1.2 equiv, 27 mg), pyrrolidine (0.38 mmol, 3 equiv, 31  $\mu$ L), trimethylsilyl azide (0.13 mmol, 1 equiv, 17  $\mu$ L) and *para*-chloro benzyl isocyanide (0.13 mmol, 1 equiv, 20 mg) in 2 ml methanol were reacted for 14 hours. The crude product was purified by SiO<sub>2</sub> column chromatography (ethyl acetate: hexane; 1:4) to obtain **14n** as brown solid (37 mg, 66 %). FTIR (KBr):  $\tilde{\nu}$  = 3063, 2953, 2924,

2853, 1493, 1449, 1411, 1113, 1017, 771, 735, 498 cm<sup>-1</sup>. <sup>1</sup>H NMR (600 MHz, CDCl<sub>3</sub>)  $\delta$  = 7.73 (d,  $J$  = 7.2 Hz, 1H), 7.66 (d,  $J$  = 7.8 Hz, 1H), 7.51 (d,  $J$  = 7.8 Hz, 1H), 7.44 – 7.42 (m, 2H), 7.33 – 7.30 (m, 2H), 7.27 – 7.25 (m, 2H), 7.16 – 7.13 (m, 1H), 6.93 (d,  $J$  = 8.4 Hz, 2H), 5.66 (d,  $J$  = 15.6 Hz, 1H), 5.07 (d,  $J$  = 15.0 Hz, 1H), 4.90 (s, 1H), 4.36 – 4.34 (m, 1H), 3.18 – 3.15 (m, 1H), 2.83 – 2.79 (m, 1H), 2.00 – 1.93 (m, 2H), 1.80 – 1.76 (m, 1H), 1.64 – 1.57 (m, 1H). <sup>13</sup>C NMR (151 MHz, CDCl<sub>3</sub>)  $\delta$  = 157.0, 143.9, 142.6, 141.1, 140.8, 134.8, 132.8, 129.4, 128.9, 128.8, 128.7, 127.7, 127.5, 126.5, 125.7, 120.2, 120.0, 64.7, 53.5, 50.1, 50.0, 31.9, 23.7 ppm. HRMS (ESI) exact mass calculated for C<sub>25</sub>H<sub>23</sub>ClN<sub>5</sub><sup>+</sup> ([M+H]<sup>+</sup>): 428.1636, found: 428.1637.

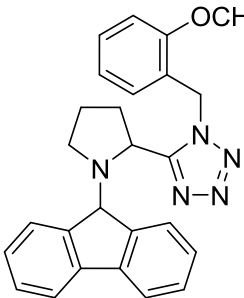
**5-(1-(9H-fluoren-9-yl)pyrrolidin-2-yl)-1-(4-fluorobenzyl)-1H-tetrazole (14o):** According to



the general procedure I: 9-fluorenone imine (0.15 mmol, 1.2 equiv, 27 mg), pyrrolidine (0.38 mmol, 3 equiv, 31  $\mu$ L), trimethylsilyl azide (0.13 mmol, 1 equiv, 17  $\mu$ L) and *para*-fluoro benzyl isocyanide (0.13 mmol, 1 equiv, 18 mg) in 2 mL methanol were reacted for 14 hours. The crude product was purified by SiO<sub>2</sub> column chromatography (ethyl acetate: hexane; 1:5) to obtain **14o** as brown solid (33 mg, 62 %). FTIR (KBr):  $\tilde{\nu}$  = 3067, 2957, 2926,

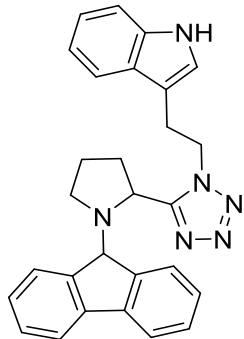
2877, 2818, 1606, 1510, 1449, 1224, 1165, 832, 776, 533, 495 cm<sup>-1</sup>. <sup>1</sup>H NMR (600 MHz, CDCl<sub>3</sub>)  $\delta$  = 7.74 (d, *J* = 7.2 Hz, 1H), 7.66 (d, *J* = 7.8 Hz, 1H), 7.54 (d, *J* = 7.2 Hz, 1H), 7.45 – 7.42 (m, 2H), 7.33 – 7.31 (m, 2H), 7.15 (t, *J* = 7.2 Hz, 1H), 7.01 – 6.96 (m, 4H), 5.65 (d, *J* = 15.6 Hz, 1H), 5.05 (d, *J* = 15.6 Hz, 1H), 4.90 (s, 1H), 4.36 – 4.34 (m, 1H), 3.21 – 3.15 (m, 1H), 2.84 – 2.80 (m, 1H), 2.01 – 1.90 (m, 2H), 1.81 – 1.76 (m, 1H), 1.63 – 1.58 (m, 1H). <sup>13</sup>C NMR (101 MHz, CDCl<sub>3</sub>)  $\delta$  = 164.1, 161.63, 156.9, 144.0, 142.7, 141.2, 140.8, 129.4, 129.3, 128.8, 128.7, 127.6, 127.5, 126.5, 125.7, 120.2, 119.9, 116.3, 116.1, 64.8, 53.6, 50.1, 50.0, 32.0, 23.7. HRMS (ESI) exact mass calculated for C<sub>25</sub>H<sub>23</sub>FN<sub>5</sub><sup>+</sup> ([M+H]<sup>+</sup>): 412.1932, found: 412.1940.

**5-(1-(9H-fluoren-9-yl)pyrrolidin-2-yl)-1-(2-methoxybenzyl)-1H-tetrazole (14p):** According to

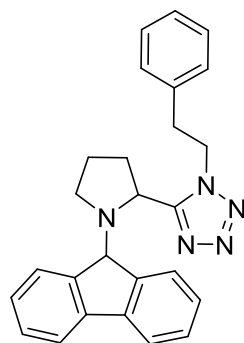


the general procedure I: 9-fluorenone imine (0.15 mmol, 1.2 equiv, 27 mg), pyrrolidine (0.38 mmol, 3 equiv, 31  $\mu$ L), trimethylsilyl azide (0.13 mmol, 1 equiv, 17  $\mu$ L) and *ortho*-methoxy benzyl isocyanide (0.13 mmol, 1 equiv, 19 mg) in 2 mL methanol were reacted for 14 hours. The crude product was purified by SiO<sub>2</sub> column chromatography (ethyl acetate: hexane; 1:4) to obtain **14p** as brown solid (36 mg, 65 %). FTIR (KBr):  $\tilde{\nu}$  = 3065, 2951,

2927, 2860, 1449, 1301, 736, 673, 621 cm<sup>-1</sup>. <sup>1</sup>H NMR (600 MHz, CDCl<sub>3</sub>)  $\delta$  = 7.71 (d, *J* = 7.8 Hz, 1H), 7.67 (d, *J* = 7.2 Hz, 1H), 7.58 (d, *J* = 7.2 Hz, 1H), 7.44 – 7.41 (m, 1H), 7.40 (d, *J* = 7.2 Hz, 1H), 7.34 – 7.29 (m, 2H), 7.27 – 7.24 (m, 1H), 7.16 – 7.13 (m, 1H), 6.86 – 6.81 (m, 3H), 5.56 (d, *J* = 15.6 Hz, 1H), 5.18 (d, *J* = 15.6 Hz, 1H), 4.93 (s, 1H), 4.45 – 4.48 (m, 1H), 3.70 (s, 3H), 3.14 – 3.11 (m, 1H), 2.78 – 2.74 (m, 1H), 2.01 – 1.97 (m, 2H), 1.77 – 1.73 (m, 2H). <sup>13</sup>C NMR (101 MHz, CDCl<sub>3</sub>)  $\delta$  = 157.2, 156.7, 144.5, 143.0, 141.1, 141.0, 130.1, 129.1, 128.62, 128.58, 127.5, 127.4, 126.5, 125.9, 122.8, 121.2, 120.1, 119.9, 110.8, 64.8, 55.5, 53.8, 49.5, 46.0, 32.0, 23.8 ppm. HRMS (ESI) exact mass calculated for C<sub>26</sub>H<sub>26</sub>N<sub>5</sub>O<sup>+</sup> ([M+H]<sup>+</sup>): 424.2132, found 424.2134.

**3-(2-(5-(1-(9H-fluoren-9-yl)pyrrolidin-2-yl)-1H-tetrazol-1-yl)ethyl)-1H-indole (14q):**

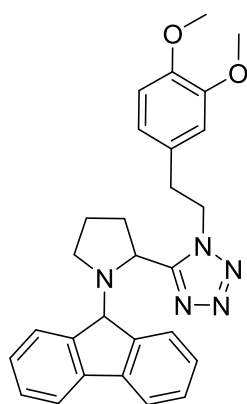
According to the general procedure I: 9-fluorenone imine (0.15 mmol, 1.2 equiv, 27 mg), pyrrolidine (0.38 mmol, 3 equiv, 31  $\mu$ L), trimethylsilyl azide (0.13 mmol, 1 equiv, 17  $\mu$ L) and 3-(2-isocyanoethyl)-1H-indole (0.13 mmol, 1 equiv, 22 mg) in 2 mL methanol were reacted for 14 hours. The crude product was purified by SiO<sub>2</sub> column chromatography (ethyl acetate: hexane; 1:4) to obtain **14q** as brown solid (46 mg, 80 %). FTIR (KBr):  $\tilde{\nu}$  = 3229, 3057, 2919, 2860, 1620, 1451, 1361, 1103, 742, 621 cm<sup>-1</sup>. <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>)  $\delta$  = 8.32 (s, 1H), 7.74 (d, *J* = 7.6 Hz, 1H), 7.63 (d, *J* = 7.6 Hz, 1H), 7.49 – 7.45 (m, 2H), 7.33 – 7.27 (m, 3H), 7.19 – 7.15 (m, 2H), 7.13 (d, *J* = 8.0 Hz, 1H), 7.05 (d, *J* = 7.2 Hz, 1H), 7.01 – 6.98 (m, 1H), 6.58 (s, 1H), 4.82 (s, 1H), 4.32 – 4.25 (m, 1H), 3.92 – 3.84 (m, 1H), 3.61 – 3.58 (m, 1H), 3.20 – 3.13 (m, 3H), 2.90 – 2.83 (m, 1H), 1.92 – 1.84 (m, 1H), 1.60 – 1.52 (m, 1H), 1.23 – 1.09 (m, 1H). <sup>13</sup>C NMR (151 MHz, CDCl<sub>3</sub>)  $\delta$  = 158.0, 144.1, 143.1, 141.0, 140.4, 136.5, 128.7, 128.5, 127.6, 127.4, 126.6, 126.2, 125.9, 123.0, 122.4, 120.0, 119.9, 119.7, 118.0, 111.6, 110.2, 64.9, 52.0, 50.9, 47.0, 31.7, 26.4, 24.0 ppm. HRMS (ESI) exact mass calculated for C<sub>28</sub>H<sub>27</sub>N<sub>6</sub><sup>+</sup> ([M+H]<sup>+</sup>): 447.2292, found: 447.2299.

**5-(1-(9H-fluoren-9-yl)pyrrolidin-2-yl)-1-phenethyl-1H-tetrazole (14r):**

According to the general procedure I: 9-fluorenone imine (0.15 mmol, 1.2 equiv, 27 mg), pyrrolidine (0.38 mmol, 3 equiv, 31  $\mu$ L), trimethylsilyl azide (0.13 mmol, 1 equiv, 17  $\mu$ L) and (2-isocyanoethyl)benzene (0.13 mmol, 1 equiv, 17 mg) in 2 mL methanol were reacted for 24 hours. The crude product was purified by SiO<sub>2</sub> column chromatography (ethyl acetate: hexane; 1:5) to obtain **14r** as light yellow solid (39 mg, 73 %). FTIR (KBr):  $\tilde{\nu}$  = 3065, 2923, 1695, 1403, 1104, 743, 668 cm<sup>-1</sup>. <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>)  $\delta$  = 7.72 (d, *J* = 7.2 Hz, 1H), 7.64 (d, *J* = 7.8 Hz, 1H), 7.54 (d, *J* = 7.2 Hz, 1H), 7.45 – 7.42 (m, 1H), 7.36 – 7.33 (m, 1H), 7.32 – 7.30 (m, 2H), 7.21 – 7.20 (m, 3H), 7.13 – 7.10 (m, 1H), 6.89 – 6.87 (m, 2H), 4.84 (s, 1H), 4.44 – 4.39 (m, 1H), 4.01 – 3.95 (m, 2H), 3.19 – 3.15 (m, 1H), 3.10 – 3.01 (m, 2H), 2.87 – 2.83 (m, 1H), 2.06 – 1.98 (m, 1H), 1.78 – 1.74 (m, 2H), 1.45 – 1.39 (m, 1H). <sup>13</sup>C NMR (151 MHz, CDCl<sub>3</sub>)  $\delta$  = 157.3, 144.1, 142.9, 141.1, 140.6, 136.8, 129.1, 128.8, 128.7, 128.6, 127.5, 127.45, 127.34, 126.3, 125.7, 120.1, 119.9, 64.8, 52.8, 50.4, 48.4, 36.3, 32.0, 24.0 ppm. HRMS (ESI) exact mass calculated for C<sub>26</sub>H<sub>26</sub>N<sub>5</sub><sup>+</sup> ([M+H]<sup>+</sup>): 408.2183, found: 408.2176.

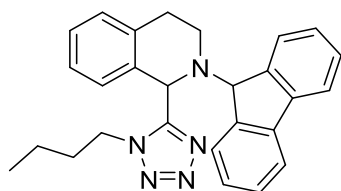


### 5-(1-(9H-fluoren-9-yl)pyrrolidin-2-yl)-1-(3,4-dimethoxyphenethyl)-1H-tetrazole (14s):



According to the general procedure I: 9-fluorenone imine (0.15 mmol, 1.2 equiv, 27 mg), pyrrolidine (0.38 mmol, 3 equiv, 31  $\mu$ L), trimethylsilyl azide (0.13 mmol, 1 equiv, 17  $\mu$ L) and 4-(2-isocyanoethyl)-1,2-dimethoxybenzene (0.123 mmol, 1equiv, 25 mg) in 2 mL methanol were reacted for 24 hours. The crude product was purified by SiO<sub>2</sub> column chromatography (ethyl acetate: hexane; 1:3) gave **14s** as light yellow solid (39 mg, 64 %). FTIR (KBr):  $\tilde{\nu}$  = 2962, 2927, 1649, 1418, 1261, 1030, 802, 742, 674, cm<sup>-1</sup>. <sup>1</sup>H NMR (600 MHz, CDCl<sub>3</sub>)  $\delta$  = 7.71 (d,  $J$  = 7.8 Hz, 1H), 7.64 (d,  $J$  = 7.8 Hz, 1H), 7.55 (d,  $J$  = 7.2 Hz, 1H), 7.43 – 7.40 (m, 1H), 7.33 (d,  $J$  = 7.8 Hz, 1H), 7.31 – 7.29 (m, 2H), 7.13 – 7.11 (m, 1H), 6.66 (d,  $J$  = 8.4 Hz, 1H), 6.41 – 6.40 (m, 1H), 6.31 (s, 1H), 4.81 (s, 1H), 4.41 – 4.37 (m, 1H), 4.01 – 3.98 (m, 1H), 3.97 – 3.92 (m, 1H), 3.79 (s, 3H), 3.70 (s, 3H), 3.16 – 3.13 (m, 1H), 3.06 – 2.97 (m, 2H), 2.85 – 2.81 (m, 1H), 2.03 – 1.99 (m, 1H), 1.78 – 1.73 (m, 2H), 1.42 – 1.39 (m, 1H). <sup>13</sup>C NMR (50 MHz, CDCl<sub>3</sub>)  $\delta$  = 157.4, 149.3, 148.3, 144.1, 142.9, 141.0, 140.6, 129.2, 128.7, 128.6, 127.5, 126.3, 125.7, 120.8, 120.1, 119.9, 111.8, 111.7, 64.7, 56.1, 56.0, 52.9, 50.2, 48.6, 35.9, 31.9, 24.0 ppm. (Total count of <sup>13</sup>C is less than expected due to the merging of signals in the aromatic region). HRMS (ESI) exact mass calculated for C<sub>28</sub>H<sub>30</sub>N<sub>5</sub><sup>+</sup>O<sub>2</sub> ([M+H]<sup>+</sup>): 468.2394, found: 468.2399.

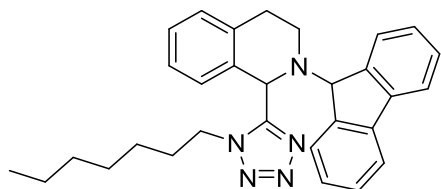
### 1-(1-butyl-1H-tetrazol-5-yl)-2-(9H-fluoren-9-yl)-1,2,3,4-tetrahydroisoquinoline(17a):



According to general procedure I: 9-fluorenone imine (0.15 mmol, 1.2 equiv, 27 mg), 1,2,3,4-tetrahydroisoquinoline (0.38 mmol, 3 equiv, 48  $\mu$ L), trimethylsilyl azide (0.13 mmol, 1 equiv, 17  $\mu$ L) and *n*-butyl isocyanide (0.13 mmol, 1 equiv, 16  $\mu$ L) in 2 mL methanol were reacted for 24 hours. The crude product was purified by SiO<sub>2</sub> column chromatography (ethyl acetate: hexane; 1:15) to obtain **17a** as white solid (46 mg, 84%). FTIR (KBr):  $\tilde{\nu}$  = 3064, 2962, 2926, 2872, 1961, 1449, 1126, 1087, 1043, 941, 777, 747, 680 cm<sup>-1</sup>. <sup>1</sup>H NMR (600 MHz, CDCl<sub>3</sub>)  $\delta$  = 7.92 (d,  $J$  = 7.2 Hz, 1H), 7.70 – 7.66 (m, 2H), 7.40 – 7.36 (m, 2H), 7.35 – 7.33 (m, 1H), 7.30 – 7.26 (m, 2H), 7.19 (t,  $J$  = 7.2 Hz, 1H), 7.13 (d,  $J$  = 7.2 Hz, 1H), 7.11 – 7.08 (m, 1H), 6.74 (d,  $J$  = 7.8 Hz, 1H), 6.46 (s, 1H), 4.56 – 4.53 (m, 1H), 4.52 (s, 1H), 4.36 – 4.31 (m, 1H), 2.97 – 2.92 (m, 1H), 2.61 – 2.58 (m, 1H), 2.51 – 2.49 (m, 2H), 1.54 – 1.48 (m, 1H), 1.14 – 1.04 (m, 3H), 0.73 (t,  $J$  = 7.2 Hz, 3H). <sup>13</sup>C NMR (151 MHz, CDCl<sub>3</sub>)  $\delta$  = 155.7, 143.8, 142.1, 141.4, 141.29, 135.2, 133.1, 129.4,

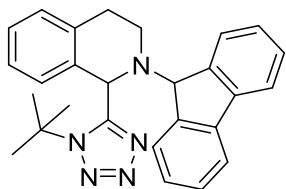
128.8, 128.7, 127.73, 127.68, 127.5, 127.3, 126.8, 126.7, 124.9, 120.4, 120.0, 66.0, 57.5, 48.1, 43.1, 30.7, 30.0, 19.9, 13.5 ppm. HRMS (ESI) exact mass calculated for  $C_{27}H_{28}N_5^+$  ( $[M+H]^+$ ): 422.2339, found: 422.2376.

**2-(9H-fluoren-9-yl)-1-(1-heptyl-1H-tetrazol-5-yl)-1,2,3,4-tetrahydroisoquinoline (17b):**



According to the general procedure I: 9-fluorenone imine (0.15 mmol, 1.2 equiv, 27 mg), 1,2,3,4-tetrahydroisoquinoline (0.38 mmol, 3 equiv, 48  $\mu$ L), trimethylsilyl azide (0.13 mmol, 1 equiv, 17  $\mu$ L) and *n*-heptyl isocyanide (0.13 mmol, 1 equiv, 16 mg) in 2 mL methanol were reacted for 17 hours. The crude product was purified by  $SiO_2$  column chromatography (ethyl acetate: hexane; 1:20) to obtain **17b** as white solid (45 mg, 75%). FTIR (KBr):  $\tilde{\nu}$  = 3443, 2956, 2926, 2856, 2827, 1469, 1449, 1290, 1127, 1086, 750, 737, 724, 677  $cm^{-1}$ .  $^1H$  NMR (600 MHz,  $CDCl_3$ )  $\delta$  = 7.91 (d,  $J$  = 7.8 Hz, 1H), 7.69 – 7.66 (m, 2H), 7.39 – 7.37 (m, 2H), 7.34 (d,  $J$  = 7.2 Hz, 1H), 7.30 – 7.24 (m, 2H), 7.20 – 7.18 (m, 1H), 7.13 (d,  $J$  = 7.2 Hz, 1H), 7.11 – 7.07 (m, 1H), 6.74 (d,  $J$  = 7.8 Hz, 1H), 6.47 (s, 1H), 4.56 – 4.52 (m, 1H), 4.51 (s, 1H), 4.36 – 4.31 (m, 1H), 2.97 – 2.92 (m, 1H), 2.61 – 2.58 (m, 1H), 2.51 – 2.49 (m, 2H), 1.56 – 1.50 (m, 1H), 1.25 – 1.21 (m, 3H), 1.12 – 1.08 (m, 3H), 1.08 – 1.05 (m, 3H), 0.86 (t,  $J$  = 7.2 Hz, 3H).  $^{13}C$  NMR (151 MHz,  $CDCl_3$ )  $\delta$  = 155.7, 143.8, 142.1, 141.4, 141.3, 135.2, 133.1, 129.4, 128.8, 128.7, 127.7, 127.6, 127.5, 127.3, 126.8, 126.7, 124.8, 120.4, 119.9, 66.0, 57.5, 48.4, 43.0, 31.6, 29.9, 28.8, 28.7, 26.6, 22.6, 14.2 ppm. HRMS (ESI) exact mass calculated for  $C_{30}H_{34}N_5^+$  ( $[M+H]^+$ ): 464.2809, found: 464.2821.

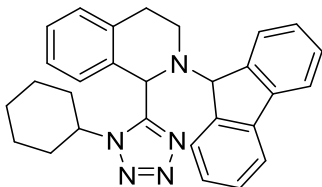
**1-(1-(tert-butyl)-1H-tetrazol-5-yl)-2-(9H-fluoren-9-yl)-1,2,3,4-tetrahydroisoquinoline (17c):**



According to the general procedure I: 9-fluorenone imine (0.15 mmol, 1.2 equiv, 27 mg), 1,2,3,4-tetrahydroisoquinoline (0.38 mmol, 3 equiv, 48  $\mu$ L), trimethylsilyl azide (0.13 mmol, 1 equiv, 17  $\mu$ L) and *tert*-butyl isocyanide (0.13 mmol, 1 equiv, 16  $\mu$ L) in 2 mL methanol were reacted for 24 hours. The crude product was purified by  $SiO_2$  column chromatography (ethyl acetate: hexane; 1:15) to obtain **17c** as white solid (47 mg, 86%). FTIR (KBr):  $\tilde{\nu}$  = 3061, 3021, 2977, 2942, 1476, 1450, 1405, 1369, 1301, 1239, 1122, 739, 726, 678, 424  $cm^{-1}$ .  $^1H$  NMR (600 MHz,  $CDCl_3$ )  $\delta$  = 8.20 (s, 1H), 7.68 (t,  $J$  = 8.4 Hz, 2H), 7.54 (d,  $J$  = 7.2 Hz, 1H), 7.40 – 7.36 (m, 2H), 7.30 (t,  $J$  = 7.2 Hz, 2H), 7.16 (t,  $J$  = 7.2 Hz, 1H), 7.09 – 7.06 (m, 2H), 6.70 (s, 1H), 6.53 (d,  $J$  = 7.8 Hz, 1H),

4.52 (s, 1H), 2.92 – 2.88 (m, 1H), 2.53 – 2.48 (m, 2H), 2.41 – 2.38 (m, 1H), 1.67 (s, 9H) ppm.  $^{13}\text{C}$  NMR (151 MHz,  $\text{CDCl}_3$ )  $\delta$  = 154.9, 143.9, 141.7, 141.4, 135.4, 135.1, 129.3, 128.7, 128.6, 127.7, 127.5, 127.4, 126.5, 126.3, 124.9, 120.2, 119.9, 66.0, 63.8, 59.8, 43.0, 30.7, 29.1 ppm. (Total count of  $^{13}\text{C}$  is less than expected due to the merging of signals in the aromatic region). HRMS (ESI) exact mass calculated for  $\text{C}_{27}\text{H}_{28}\text{N}_5^+([\text{M}+\text{H}]^+)$ : 422.2339, found: 422.2318.

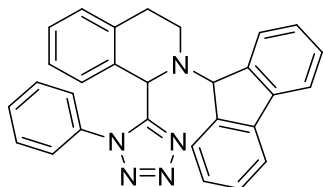
**1-(1-cyclohexyl-1H-tetrazol-5-yl)-2-(9H-fluoren-9-yl)-1,2,3,4-tetrahydroisoquinoline (17d):**



According to general procedure: 9-fluorenone imine (0.15 mmol, 1.2 equiv, 27 mg), 1,2,3,4-tetrahydroisoquinoline (0.38 mmol, 3 equiv, 48  $\mu\text{L}$ ), trimethylsilyl azide (0.13 mmol, 1 equiv, 17  $\mu\text{L}$ ) and cyclohexyl isocyanide (0.13 mmol, 1 equiv, 16  $\mu\text{L}$ ) in 2 mL methanol

were reacted for 24 hours. The crude product was purified by  $\text{SiO}_2$  column chromatography (ethyl acetate: hexane; 1:3) to obtain **17d** as white solid (52 mg, 89%). FTIR (KBr):  $\tilde{\nu}$  = 3060, 2938, 1948, 1450, 1434, 742, 724, 622  $\text{cm}^{-1}$ .  $^1\text{H}$  NMR (600 MHz,  $\text{CDCl}_3$ )  $\delta$  = 8.02 (d,  $J$  = 7.8 Hz, 1H), 7.71 – 7.67 (m, 2H), 7.40 – 7.38 (m, 2H), 7.35 – 7.34 (m, 1H), 7.31 – 7.27 (m, 2H), 7.19 – 7.17 (m, 1H), 7.13 – 7.12 (m, 1H), 7.10 – 7.08 (m, 1H), 6.71 (d,  $J$  = 8.4 Hz, 1H), 6.53 (s, 1H), 4.76 – 4.71 (m, 1H), 4.57 (s, 1H), 3.00 – 2.93 (m, 1H), 2.60 – 2.57 (m, 1H), 2.47 – 2.38 (m, 2H), 2.25 – 2.21 (m, 2H), 2.08 – 2.06 (m, 1H), 1.68 – 1.67 (m, 1H), 1.59 (d,  $J$  = 16.2 Hz, 1H), 1.48 – 1.41 (m, 2H), 1.28 – 1.25 (m, 1H), 0.88 – 0.82 (m, 1H), 0.72 – 0.70 (m, 1H).  $^{13}\text{C}$  NMR (151 MHz,  $\text{CDCl}_3$ )  $\delta$  = 155.0, 144.0, 142.1, 141.5, 141.4, 135.3, 133.4, 129.3, 128.8, 128.7, 127.7, 127.5, 127.4, 127.1, 126.7, 124.4, 120.4, 120.0, 65.8, 58.6, 57.7, 42.6, 32.9, 32.3, 30.1, 25.9, 25.6, 25.1 ppm (Total count of  $^{13}\text{C}$  is less than expected due to the merging of signals in the aromatic region). HRMS (ESI) exact mass calculated for  $\text{C}_{29}\text{H}_{30}\text{N}_5^+([\text{M}+\text{H}]^+)$ : 448.2496, found: 448.2484.

**2-(9H-fluoren-9-yl)-1-(1-phenyl-1H-tetrazol-5-yl)-1,2,3,4-tetrahydroisoquinoline (17e):**

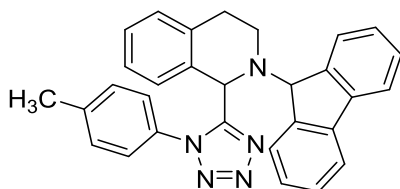


According to general procedure: 9-fluorenone imine (0.15 mmol, 1.2 equiv, 27 mg), 1,2,3,4-tetrahydroisoquinoline (0.38 mmol, 3 equiv, 48  $\mu\text{L}$ ), trimethylsilyl azide (0.13 mmol, 1 equiv, 17  $\mu\text{L}$ ) and phenyl isocyanide (0.13 mmol, 1 equiv, 14 mg) in 2 mL methanol were reacted

for 12 hours. The crude product was purified by  $\text{SiO}_2$  column chromatography (ethyl acetate: hexane; 1:20) to obtain **17e** as white solid (41 mg, 71%). FTIR (KBr):  $\tilde{\nu}$  = 3062, 2969, 2895, 2847, 1595, 1493, 1450, 1264, 1080, 756, 742, 686, 534  $\text{cm}^{-1}$ .  $^1\text{H}$  NMR (600 MHz,  $\text{CDCl}_3$ )  $\delta$  = 7.89 (d,

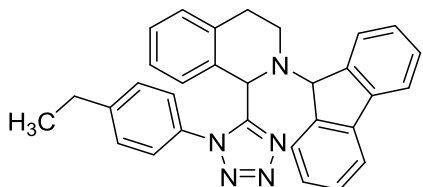
$J = 7.2$  Hz, 1H), 7.67 (d,  $J = 7.8$  Hz, 1H), 7.61 (d,  $J = 7.8$  Hz, 1H), 7.47 – 7.45 (m, 1H), 7.37– 7.35 (m, 3H), 7.33 – 7.31 (m, 1H), 7.27 – 7.24 (m, 1H), 7.21 (d,  $J = 8.4$  Hz, 2H), 7.15 – 7.13 (m, 2H), 7.11 – 7.08 (m, 1H), 6.99 (d,  $J = 7.8$  Hz, 1H), 6.86 (d,  $J = 7.8$  Hz, 1H), 6.75 (d,  $J = 7.8$  Hz, 1H), 6.57 (s, 1H), 4.61 (s, 1H), 2.56 – 2.50 (m, 1H), 2.38 – 2.37 (m, 3H).  $^{13}\text{C}$  NMR (151 MHz,  $\text{CDCl}_3$ )  $\delta = 156.1, 143.7, 142.2, 141.5, 141.1, 135.7, 135.0, 133.5, 130.1, 129.3, 129.0, 128.7, 128.6, 127.7, 127.5, 127.3, 127.0, 126.8, 126.6, 125.7, 125.0, 120.4, 119.7, 65.9, 57.8, 42.7, 29.4$  ppm. HRMS (ESI) exact mass calculated for  $\text{C}_{29}\text{H}_{24}\text{N}_5^+$  ( $[\text{M}+\text{H}]^+$ ): 442.2026, found: 442.2020.

**2-(9H-fluoren-9-yl)-1-(1-(p-tolyl)-1H-tetrazol-5-yl)-1,2,3,4-tetrahydroisoquinoline (17f):**



According to the general procedure I: 9-fluorenone imine (0.15 mmol, 1.2 equiv, 27 mg), 1,2,3,4-tetrahydroisoquinoline (0.38 mmol, 3 equiv, 48  $\mu\text{L}$ ), trimethylsilyl azide (0.13 mmol, 1 equiv, 17  $\mu\text{L}$ ) and *para*-methyl phenyl isocyanide (0.13 mmol, 1 equiv, 15 mg) in 2 mL methanol were reacted for 14 hours. The crude product was purified by  $\text{SiO}_2$  column chromatography (ethyl acetate: hexane; 1:20) to obtain **17f** as white solid (41 mg, 70%). FTIR (KBr):  $\tilde{\nu} = 3066, 2929, 2848, 1904, 1650, 1450, 1433, 1384, 1260, 1073, 823, 738, 723, 535$   $\text{cm}^{-1}$ .  $^1\text{H}$  NMR (600 MHz,  $\text{CDCl}_3$ )  $\delta = 7.87$  (d,  $J = 7.8$  Hz, 1H), 7.68 (d,  $J = 7.8$  Hz, 1H), 7.62 (d,  $J = 7.8$  Hz, 1H), 7.37 – 7.32 (m, 2H), 7.27 – 7.24 (m, 1H), 7.17 – 7.14 (m, 4H), 7.11 – 7.07 (m, 3H), 7.01 (d,  $J = 7.2$  Hz, 1H), 6.86 (d,  $J = 7.8$  Hz, 1H), 6.77 (d,  $J = 7.2$  Hz, 1H), 6.54 (s, 1H), 4.61 (s, 1H), 2.59 – 2.53 (m, 1H), 2.42 (s, 3H), 2.41 – 2.39 (m, 3H).  $^{13}\text{C}$  NMR (151 MHz,  $\text{CDCl}_3$ )  $\delta = 156.2, 143.8, 142.4, 141.5, 141.1, 140.3, 135.8, 133.7, 132.5, 129.5, 129.3, 128.6, 128.6, 127.6, 127.5, 127.3, 127.0, 126.8, 126.6, 125.5, 125.1, 120.4, 119.7, 66.1, 57.7, 42.8, 29.5, 21.4$  ppm. HRMS (ESI) exact mass calculated for  $\text{C}_{30}\text{H}_{26}\text{N}_5^+$  ( $[\text{M}+\text{H}]^+$ ): 456.2183, found: 456.2181.

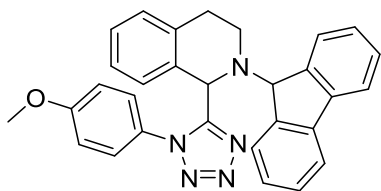
**1-(1-(4-ethylphenyl)-1H-tetrazol-5-yl)-2-(9H-fluoren-9-yl)-1,2,3,4-**



**tetrahydroisoquinoline(17g):** According to the general procedure I: 9-fluorenone imine (0.15 mmol, 1.2 equiv, 27 mg), 1,2,3,4-tetrahydroisoquinoline (0.38 mmol, 3 equiv, 48  $\mu\text{L}$ ), trimethylsilyl azide (0.13 mmol, 1 equiv, 17  $\mu\text{L}$ ) and *para*-ethyl phenyl isocyanide (0.13 mmol, 1 equiv, 17 mg) in 2 mL methanol were reacted for 12 hours. The crude product was purified by  $\text{SiO}_2$  column chromatography (ethyl acetate: hexane; 1:20) to obtain **17g** as white solid (44 mg, 72%). FTIR (KBr):  $\tilde{\nu} = 3062, 2960, 2835, 1517, 1449, 1259,$

839, 751, 739, 552 cm<sup>-1</sup>. <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>) δ = 7.86 (d, *J* = 7.2 Hz, 1H), 7.67 (d, *J* = 7.6 Hz, 1H), 7.61 (d, *J* = 7.6 Hz, 1H), 7.37 – 7.29 (m, 2H), 7.25 – 7.22 (m, 1H), 7.19 – 7.15 (m, 2H), 7.19 – 7.08 (m, 5H), 7.00 (d, *J* = 7.6 Hz, 1H), 6.88 (d, *J* = 7.6 Hz, 1H), 6.68 (d, *J* = 7.6 Hz, 1H), 6.55 (s, 1H), 4.58 (s, 1H), 2.73 – 2.68 (m, 2H), 2.60 – 2.52 (m, 1H), 2.41 – 2.37 (m, 3H), 1.28 (t, *J* = 7.6 Hz, 3H). <sup>13</sup>C NMR (101 MHz, CDCl<sub>3</sub>) δ = 156.1, 146.7, 143.8, 142.3, 141.4, 141.0, 135.7, 133.7, 132.6, 129.3, 128.6, 128.5, 128.4, 127.6, 127.5, 127.3, 127.0, 126.8, 126.6, 125.6, 125.1, 120.3, 119.7, 65.9, 57.8, 42.7, 29.4, 28.8, 16.0. HRMS (ESI) exact mass calculated for C<sub>31</sub>H<sub>28</sub>N<sub>5</sub><sup>+</sup> ([M+H]<sup>+</sup>): 470.2339, found: 470.2342.

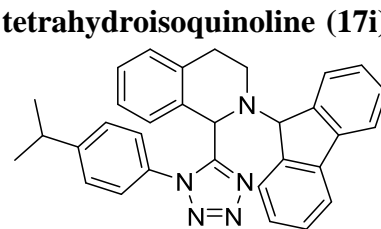
### 2-(9H-fluoren-9-yl)-1-(1-(4-methoxyphenyl)-1H-tetrazol-5-yl)-1,2,3,4-



**tetrahydroisoquinoline (17h):** According to the general procedure I: 9-fluorenone imine (0.15 mmol, 1.2 equiv, 27 mg), 1,2,3,4-tetrahydroisoquinoline (0.38 mmol, 3 equiv, 48 μL), trimethylsilyl azide (0.13 mmol, 1 equiv, 17 μL) and *para*-

methoxy phenyl isocyanide (0.13 mmol, 1 equiv, 17 mg) in 2 mL methanol were reacted for 14 hours. The crude product was purified by SiO<sub>2</sub> column chromatography (ethyl acetate: hexane; 1:6) to obtain **17h** as white solid (51 mg, 84%). FTIR (KBr):  $\tilde{\nu}$  = 3064, 3010, 2909, 2841, 1607, 1517, 1449, 1301, 1253, 1082, 1024, 834, 741, 726, 620, 539 cm<sup>-1</sup>. <sup>1</sup>H NMR (600 MHz, CDCl<sub>3</sub>) δ = 7.88 (d, *J* = 7.8 Hz, 1H), 7.68 (d, *J* = 7.8 Hz, 1H), 7.63 (d, *J* = 7.2 Hz, 1H), 7.38 – 7.32 (m, 2H), 7.27 – 7.24 (m, 1H), 7.18 – 7.13 (m, 2H), 7.11 – 7.08 (m, 3H), 7.00 (d, *J* = 7.2 Hz, 1H), 6.88 – 6.83 (m, 4H), 6.53 (s, 1H), 4.63 (s, 1H), 3.85 (s, 3H), 2.57 – 2.51 (m, 1H), 2.41 – 2.36 (m, 3H). <sup>13</sup>C NMR (151 MHz, CDCl<sub>3</sub>) δ = 160.7, 156.3, 143.8, 142.3, 141.5, 141.1, 135.8, 133.6, 129.3, 128.64, 128.58, 127.8, 127.6, 127.5, 127.3, 127.1, 127.0, 126.8, 126.6, 125.1, 120.4, 119.8, 114.1, 66.0, 57.6, 55.9, 42.7, 29.5 ppm. HRMS (ESI) exact mass calculated for C<sub>30</sub>H<sub>26</sub>N<sub>5</sub>O<sup>+</sup> ([M+H]<sup>+</sup>): 472.2131, found: 472.2134.

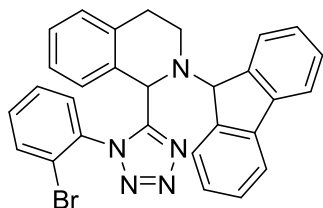
### 2-(9H-fluoren-9-yl)-1-(1-(4-isopropylphenyl)-1H-tetrazol-5-yl)-1,2,3,4-



**tetrahydroisoquinoline (17i):** According to the general procedure I: 9-fluorenone imine (0.15 mmol, 1.2 equiv, 27 mg), 1,2,3,4-tetrahydroisoquinoline (0.38 mmol, 3 equiv, 48 μL), trimethylsilyl azide (0.13 mmol, 1 equiv, 17 μL) and *para*-isopropyl phenyl isocyanide (0.13 mmol, 1 equiv, 19 mg) in 2 mL methanol were reacted for 16 hours. The

crude product was purified by SiO<sub>2</sub> column chromatography (ethyl acetate: hexane; 1:20) to obtain **17i** as grey solid (48 mg, 77%). FTIR (KBr):  $\tilde{\nu}$  = 3059, 3037, 2961, 2926, 2850, 1821, 1518, 1449, 1421, 1266, 1137, 1075, 835, 747, 725, 556 cm<sup>-1</sup>. <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>)  $\delta$  = 7.85 (d, *J* = 7.6 Hz, 1H), 7.67 (d, *J* = 7.2 Hz, 1H), 7.60 (d, *J* = 7.6 Hz, 1H), 7.37 – 7.29 (m, 2H), 7.24 – 7.20 (m, 2H), 7.17 – 7.09 (m, 5H), 7.01 (d, *J* = 7.6 Hz, 1H), 6.89 (d, *J* = 7.2 Hz, 1H), 6.60 – 6.54 (m, 2H), 4.56 (s, 1H), 3.01 – 2.94 (m, 1H), 2.61 – 2.53 (m, 1H), 2.41 – 2.35 (m, 3H), 1.29 (d, *J* = 6.4 Hz, 6H). <sup>13</sup>C NMR (151 MHz, CDCl<sub>3</sub>)  $\delta$  = 156.0, 151.3, 143.7, 142.2, 141.4, 141.0, 135.6, 133.7, 132.6, 129.3, 128.6, 128.5, 127.6, 127.4, 127.3, 127.0, 126.9, 126.8, 126.6, 125.6, 125.0, 120.3, 119.7, 65.9, 57.9, 42.7, 42.2, 34.2, 29.4, 24.2, 24.1 ppm. HRMS (ESI) exact mass calculated for C<sub>32</sub>H<sub>30</sub>N<sub>5</sub><sup>+</sup> ([M+H]<sup>+</sup>): 484.2496, found: 484.2497.

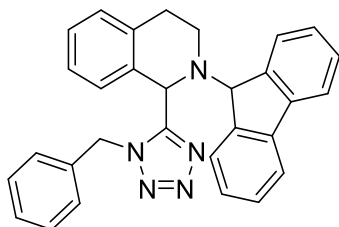
### 1-(1-(2-bromophenyl)-1H-tetrazol-5-yl)-2-(9H-fluoren-9-yl)-1,2,3,4-tetrahydroisoquinoline



**(17j):** According to the general procedure: 9-fluorenone imine (0.15 mmol, 1.2 equiv, 27 mg), 1,2,3,4-tetrahydroisoquinoline (0.38 mmol, 3 equiv, 48  $\mu$ L), trimethylsilyl azide (0.13 mmol, 1 equiv, 17  $\mu$ L) and *ortho*-bromo phenyl isocyanide (0.13 mmol, 1 equiv, 24 mg) in 2 mL

methanol were reacted for 14 hours. The crude product was purified by SiO<sub>2</sub> column chromatography (ethyl acetate: hexane; 1:20) to obtain **17j** as brown gummy compound (44 mg, 65%). FTIR (KBr):  $\tilde{\nu}$  = 3062, 2969, 2895, 2847, 1595, 1493, 1450, 1264, 1080, 756, 742, 686 cm<sup>-1</sup>. <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>)  $\delta$  = 7.91 (d, *J* = 7.2 Hz, 1H), 7.73 – 7.79 (m, 2H), 7.66 (d, *J* = 7.6 Hz, 1H), 7.39 – 7.34 (m, 3H), 7.28 – 7.24 (m, 2H), 7.22 – 7.18 (m, 2H), 7.16 – 7.13 (m, 2H), 7.07 (d, *J* = 7.6 Hz, 1H), 6.94 – 6.92 (m, 2H), 6.51 (s, 1H), 4.89 (s, 1H), 2.40 – 2.22 (m, 4H). <sup>13</sup>C NMR (101 MHz, CDCl<sub>3</sub>)  $\delta$  = 156.9, 143.8, 142.4, 141.6, 141.2, 136.0, 134.1, 134.0, 133.4, 132.0, 129.1, 129.0, 128.7, 128.6, 127.72, 127.70, 127.5, 127.4, 127.3, 127.0, 126.8, 125.4, 121.6, 120.3, 119.8, 66.4, 57.6, 42.3, 29.3. HRMS (ESI) exact mass calculated for C<sub>29</sub>H<sub>23</sub>BrN<sub>5</sub><sup>+</sup> ([M+H]<sup>+</sup>): 520.1133, found: 520.1123.

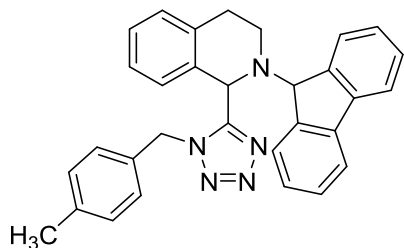
### 1-(1-benzyl-1H-tetrazol-5-yl)-2-(9H-fluoren-9-yl)-1,2,3,4-tetrahydroisoquinoline (17k):



According to the general procedure I: 9-fluorenone imine (0.15 mmol, 1.2 equiv, 27 mg), 1,2,3,4-tetrahydroisoquinoline (0.38 mmol, 3 equiv, 48  $\mu$ L), trimethylsilyl azide (0.13 mmol, 1 equiv, 17  $\mu$ L) and benzyl isocyanide (0.13 mmol, 1 equiv, 15 mg) in 2 mL methanol

were reacted for 12 hours. The crude product was purified by SiO<sub>2</sub> column chromatography (ethyl acetate: hexane; 1:20) to obtain **17k** as white solid (56 mg, 95%). FTIR (KBr):  $\tilde{\nu}$  = 3063, 2933, 2899, 1497, 1449, 1132, 1157, 1084, 773, 743, 725, 692, 678, 621 cm<sup>-1</sup>. <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>)  $\delta$  = 7.90 (d, *J* = 7.6 Hz, 1H), 7.70 – 7.66 (m, 2H), 7.40 – 7.35 (m, 2H), 7.28 – 7.17 (m, 4H), 7.14 – 7.10 (m, 4H), 6.90 – 6.86 (m, 1H), 6.75 (d, *J* = 7.6 Hz, 2H), 6.47 (d, *J* = 7.6 Hz, 1H), 6.40 (s, 1H), 5.74 (d, *J* = 14.8 Hz, 1H), 5.41 (d, *J* = 14.8 Hz, 1H), 4.54 (s, 1H), 3.05 – 2.97 (m, 1H), 2.65 – 2.52 (m, 3H). <sup>13</sup>C NMR (151 MHz, CDCl<sub>3</sub>)  $\delta$  = 155.8, 143.6, 142.1, 141.4, 141.3, 135.0, 133.3, 132.9, 129.4, 128.84, 128.82, 128.77, 128.5, 128.2, 127.8, 127.7, 127.5, 127.4, 126.81, 126.77, 125.1, 120.4, 119.9, 66.3, 57.1, 51.6, 43.4, 29.9 ppm. HRMS (ESI) exact mass calculated for C<sub>30</sub>H<sub>26</sub>N<sub>5</sub><sup>+</sup> ([M+H]<sup>+</sup>): 456.2183, found: 456.2187.

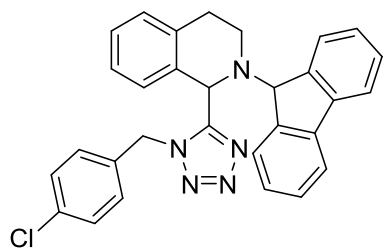
### 2-(9H-fluoren-9-yl)-1-(1-(4-methylbenzyl)-1H-tetrazol-5-yl)-1,2,3,4-tetrahydroisoquinoline



**(17l):** According to the general procedure I: 9-fluorenone imine (0.15 mmol, 1.2 equiv, 27 mg), 1,2,3,4-tetrahydroisoquinoline (0.38 mmol, 3 equiv, 48  $\mu$ L), trimethylsilyl azide (0.13 mmol, 1 equiv, 17  $\mu$ L) and *para*-methyl benzyl isocyanide (0.13 mmol, 1 equiv, 17 mg) in 2 mL methanol were reacted for 16 hours.

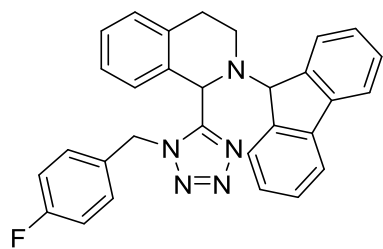
The crude product was purified by SiO<sub>2</sub> column chromatography (ethyl acetate: hexane; 1:20) to obtain **17l** as white solid (48 mg, 79%). FTIR (KBr):  $\tilde{\nu}$  = 3054, 2960, 2919, 2815, 1447, 1287, 1126, 1041, 741, 725, 622, 476 cm<sup>-1</sup>. <sup>1</sup>H NMR (600 MHz, CDCl<sub>3</sub>)  $\delta$  = 7.91 (d, *J* = 7.2 Hz, 1H), 7.71 – 7.68 (m, 2H), 7.41 – 7.37 (m, 2H), 7.28 – 7.23 (m, 2H), 7.19 – 7.16 (m, 1H), 7.14 – 7.11 (m, 2H), 6.95 – 6.92 (m, 3H), 6.64 (d, *J* = 7.8 Hz, 2H), 6.49 (d, *J* = 7.2 Hz, 1H), 6.41 (s, 1H), 5.68 (d, *J* = 14.4 Hz, 1H), 5.34 (d, *J* = 14.4 Hz, 1H), 4.56 (s, 1H), 3.04 – 3.00 (m, 1H), 2.66 – 2.63 (m, 2H), 2.58 – 2.56 (m, 1H), 2.27 (s, 3H). <sup>13</sup>C NMR (151 MHz, CDCl<sub>3</sub>)  $\delta$  = 155.7, 143.7, 142.2, 141.4, 141.3, 138.4, 135.1, 133.1, 130.4, 129.5, 129.4, 128.8, 128.7, 128.4, 127.7, 127.5, 127.4, 126.8, 125.2, 120.4, 119.9, 66.3, 57.2, 51.6, 43.4, 30.0, 21.3 ppm (Total count of <sup>13</sup>C is less than expected due to the merging of signals in the aromatic region). HRMS (ESI) exact mass calculated for C<sub>31</sub>H<sub>28</sub>N<sub>5</sub><sup>+</sup> ([M+H]<sup>+</sup>): 470.2339, found: 470.2341.

### 1-(1-(4-chlorobenzyl)-1H-tetrazol-5-yl)-2-(9H-fluoren-9-yl)-1,2,3,4-tetrahydroisoquinoline



**(17m):** According to the general procedure I: 9-fluorenone imine (0.15 mmol, 1.2 equiv, 27 mg), 1,2,3,4-tetrahydroisoquinoline (0.38 mmol, 3 equiv, 48  $\mu$ L), trimethylsilyl azide (0.13 mmol, 1 equiv, 17  $\mu$ L) and *para*-chloro benzyl isocyanide (0.13 mmol, 1 equiv, 20 mg) in 2 mL methanol were reacted for 16 hours. The crude product was purified by SiO<sub>2</sub> column chromatography (ethyl acetate: hexane; 1:20) to obtain **17m** as white solid (61 mg, 96%). FTIR (KBr):  $\tilde{\nu}$  = 3101, 3031, 2961, 2816, 1590, 1493, 1448, 1126, 740, 725, 511, 442 cm<sup>-1</sup>. <sup>1</sup>H NMR (600 MHz, CDCl<sub>3</sub>)  $\delta$  = 7.90 (d, *J* = 7.2 Hz, 1H), 7.70 – 7.67 (m, 2H), 7.40 – 7.37 (m, 2H), 7.28 – 7.25 (m, 2H), 7.21 – 7.20 (m, 1H), 7.15 – 7.12 (m, 1H), 7.10 – 7.07 (m, 3H), 7.21 – 7.20 (m, 1H), 6.91 – 6.87 (m, 2H), 6.50 (d, *J* = 8.4 Hz, 1H), 6.44 (s, 1H), 5.78 (d, *J* = 15.0 Hz, 1H), 5.45 (d, *J* = 15.0 Hz, 1H), 4.51 (s, 1H), 3.02 – 2.96 (m, 1H), 2.63 – 2.62 (m, 1H), 2.55 – 2.53 (m, 2H). <sup>13</sup>C NMR (151 MHz, CDCl<sub>3</sub>)  $\delta$  = 155.8, 143.5, 141.9, 141.4, 141.3, 134.9, 134.5, 132.8, 131.7, 129.6, 129.5, 128.9, 128.8, 127.8, 127.7, 127.5, 127.4, 126.9, 126.7, 124.9, 120.5, 120.0, 66.1, 57.3, 50.9, 43.2, 29.9 ppm. (Total count of <sup>13</sup>C is less than expected due to the merging of signals in the aromatic region). HRMS (ESI) exact mass calculated for C<sub>30</sub>H<sub>25</sub>ClN<sub>5</sub><sup>+</sup> ([M+H]<sup>+</sup>): 490.1793, found: 490.1792.

### 2-(9H-fluoren-9-yl)-1-(1-(4-fluorobenzyl)-1H-tetrazol-5-yl)-1,2,3,4-tetrahydroisoquinoline

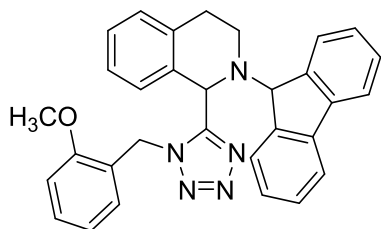


**(17n):** According to the general procedure I: 9-fluorenone imine (0.15 mmol, 1.2 equiv, 27 mg), 1,2,3,4-tetrahydroisoquinoline (0.38 mmol, 3 equiv, 48  $\mu$ L), trimethylsilyl azide (0.13 mmol, 1 equiv, 17  $\mu$ L) and *para*-fluoro benzyl isocyanide (0.13 mmol, 1 equiv, 18 mg) in 2 mL methanol were reacted for 14 hours. After completion of the reaction, the solid product was precipitated from the reaction mixture. Then, the solid product was filtered and washed with (3 $\times$ 5 mL) methanol to get the desired product (48 mg) as white solid. Next, mother liquor was evaporated under reduced pressure and residue was purified by column chromatography (Ethyl acetate: hexane; 1:10) to give an additional amount (7 mg) of the product. The combined yield is (55 mg, 89%). FTIR (KBr):  $\tilde{\nu}$  = 3065, 2926, 2836, 1605, 1510, 1450, 1225, 1158, 745, 773, 677, 538 cm<sup>-1</sup>. <sup>1</sup>H NMR (600 MHz, CDCl<sub>3</sub>)  $\delta$  = 7.90 (d, *J* = 7.8 Hz, 1H), 7.70 – 7.67 (m, 2H), 7.40 – 7.36 (m, 2H), 7.28 – 7.25 (m, 4H), 7.14 – 7.10 (m, 2H), 6.93 – 6.88 (m, 1H), 6.80 – 6.77 (m, 2H), 6.71 – 6.85 (m, 2H), 6.49 (d, *J* = 7.8 Hz, 1H), 6.43 (s, 1H),



5.77 (d,  $J = 15.0$  Hz, 1H), 5.45 (d,  $J = 14.4$  Hz, 1H), 4.52 (s, 1H), 3.04 – 2.98 (m, 1H), 2.66 – 2.63 (m, 1H), 2.58 – 2.55 (m, 2H).  $^{13}\text{C}$  NMR (101 MHz,  $\text{CDCl}_3$ )  $\delta = 155.7, 143.6, 142.0, 141.4, 141.3, 135.0, 133.0, 130.3, 130.2, 129.5, 129.1, 128.9, 128.8, 127.8, 127.7, 127.6, 127.4, 126.9, 126.7, 125.0, 120.5, 120.0, 115.8, 115.6, 66.3, 57.3, 50.9, 43.4, 30.0$  ppm. HRMS (ESI) exact mass calculated for  $\text{C}_{30}\text{H}_{25}\text{FN}_5^+$  ( $[\text{M}+\text{H}]^+$ ): 474.2089, found: 474.2088.

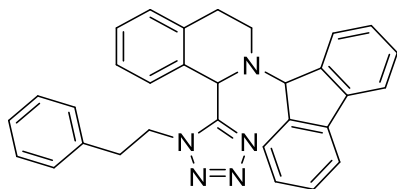
### 2-(9H-fluoren-9-yl)-1-(1-(2-methoxybenzyl)-1H-tetrazol-5-yl)-1,2,3,4-



**tetrahydroisoquinoline (17o):** According to the general procedure I: 9-fluorenone imine (0.15 mmol, 1.2 equiv, 27 mg), 1,2,3,4-tetrahydroisoquinoline (0.38 mmol, 3 equiv, 48  $\mu\text{L}$ ), trimethylsilyl azide (0.13 mmol, 1 equiv, 17  $\mu\text{L}$ ) and *ortho*-methoxy benzyl isocyanide (0.13 mmol, 1 equiv, 17 mg) in 2 mL

methanol were reacted for 14 hours. After completion of the reaction, the solid product was precipitated from the reaction mixture. Then, the solid product was washed with (3 $\times$ 5 mL) methanol to get the desired product (53 mg) as white solid. Next, mother liquor was evaporated under reduced pressure and residue was purified by column chromatography (Ethyl acetate: hexane; 1:10) to give an additional amount (7 mg) of the product. The combined yield is (60 mg, 95%). FTIR (KBr):  $\tilde{\nu} = 3067, 2957, 2926, 1606, 1510, 1449, 1224, 1165, 1111, 832, 733, 533, 495$   $\text{cm}^{-1}$ .  $^1\text{H}$  NMR (600 MHz,  $\text{CDCl}_3$ )  $\delta$  7.92 (d,  $J = 7.2$  Hz, 1H), 7.73 – 7.70 (m, 2H), 7.42 – 7.38 (m, 2H), 7.32 – 7.31 (m, 1H), 7.29 – 7.27 (m, 2H), 7.22 – 7.20 (m, 1H), 7.06 – 7.01 (m, 2H), 6.92 – 6.90 (m, 1H), 6.78 (d,  $J = 7.8$  Hz, 1H), 6.74 – 6.71 (m, 1H), 6.55 (d,  $J = 7.2$  Hz, 2H), 6.41 (s, 1H), 5.63 – 5.60 (m, 1H), 5.55 – 5.53 (m, 1H), 4.66 (s, 1H), 3.70 (s, 3H), 3.00 – 2.95 (m, 1H), 2.70 – 2.51 (m, 3H).  $^{13}\text{C}$  NMR (151 MHz,  $\text{CDCl}_3$ )  $\delta = 156.6, 155.9, 143.8, 142.3, 141.4, 141.3, 135.3, 132.6, 129.7, 129.1, 128.75, 128.7, 127.7, 127.5, 127.4, 127.3, 126.8, 126.5, 125.3, 121.7, 120.7, 120.4, 119.9, 110.4, 66.5, 56.9, 55.4, 46.5, 43.3, 29.8$  ppm (Total count of  $^{13}\text{C}$  is less than expected due to the merging of signals in the aromatic region). HRMS (ESI) exact mass calculated for  $\text{C}_{31}\text{H}_{28}\text{N}_5\text{O}^+$  ( $[\text{M}+\text{H}]^+$ ): 486.2288, found: 486.2285.

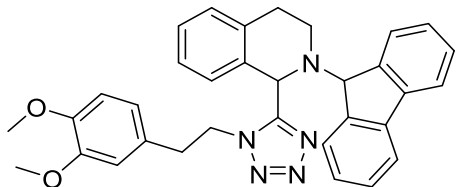
**2-(9H-fluoren-9-yl)-1-(1-phenethyl-1H-tetrazol-5-yl)-1,2,3,4-tetrahydroisoquinoline (17p):**



According to the general procedure I: 9-fluorenone imine (0.15 mmol, 1.2 equiv, 27 mg), 1,2,3,4-tetrahydroisoquinoline (0.38 mmol, 3 equiv, 48  $\mu$ L), trimethylsilyl azide (0.13 mmol, 1 equiv, 17  $\mu$ L) and (2-isocyanoethyl) benzene (0.13 mmol, 1 equiv, 17

mg) in 2 mL methanol were reacted for 24 hours. The crude product was purified by SiO<sub>2</sub> column chromatography (ethyl acetate: hexane; 1:3) to obtain **17p** as (52 mg, 89%) white solid. FTIR (KBr):  $\tilde{\nu}$  = 3062, 2961, 2820, 1494, 1138, 753, 742, 696 cm<sup>-1</sup>. <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>)  $\delta$  = 7.90 (d,  $J$  = 7.6 Hz, 1H), 7.69 – 7.65 (m, 2H), 7.39 – 7.34 (m, 2H), 7.28 – 7.22 (m, 8H), 7.16 – 7.12 (m, 1H), 6.89 (d,  $J$  = 7.2 Hz, 2H), 6.78 (d,  $J$  = 8.0 Hz, 1H), 6.47 (s, 1H), 4.81 – 4.74 (m, 1H), 4.57 – 4.85 (m, 2H), 3.01 – 2.88 (m, 2H), 2.66 – 2.62 (m, 1H), 2.57 – 2.48 (m, 2H), 2.10 – 2.02 (m, 1H). <sup>13</sup>C NMR (151 MHz, CDCl<sub>3</sub>)  $\delta$  = 155.8, 143.5, 142.0, 141.4, 141.2, 136.7, 135.3, 133.2, 129.6, 129.0, 128.9, 128.80, 128.76, 128.0, 127.72, 127.66, 127.3, 127.2, 127.1, 126.6, 125.0, 120.4, 119.9, 66.1, 57.3, 49.4, 43.3, 35.5, 30.0 ppm. HRMS (ESI) exact mass calculated for C<sub>31</sub>H<sub>28</sub>N<sub>5</sub><sup>+</sup> ([M+H]<sup>+</sup>): 470.2339, found: 470.2333.

**1-(1-(3,4-dimethoxyphenethyl)-1H-tetrazol-5-yl)-2-(9H-fluoren-9-yl)-1,2,3,4-**

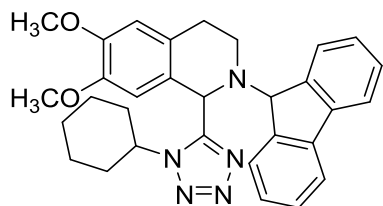


**tetrahydroisoquinoline (17q):** According to the general procedure I: 9-fluorenone imine (0.15 mmol, 1.2 equiv, 27 mg), 1,2,3,4-tetrahydroisoquinoline (0.38 mmol, 3 equiv, 48  $\mu$ L), trimethylsilyl azide (0.13 mmol, 1 equiv, 17  $\mu$ L) and 4-

(2-isocyanoethyl)-1,2-dimethoxybenzene (0.13 mmol, 1 equiv, 25 mg) in 2 mL methanol were reacted for 24 hours. The crude product was purified by SiO<sub>2</sub> column chromatography (ethyl acetate: hexane; 1:3) to obtain **17q** as white solid (64 mg, 93%). FTIR (KBr):  $\tilde{\nu}$  = 3414, 2962, 2927, 1649, 1418, 1261, 1030, 802, 742, 674 cm<sup>-1</sup>. <sup>1</sup>H NMR (600 MHz, CDCl<sub>3</sub>)  $\delta$  = 7.90 (d,  $J$  = 7.2 Hz, 1H), 7.69 (d,  $J$  = 7.8 Hz, 1H), 7.66 (d,  $J$  = 7.8 Hz, 1H), 7.39 – 7.35 (m, 2H), 7.28 – 7.24 (m, 3H), 7.23 – 7.21 (m, 2H), 7.15 – 7.13 (m, 1H), 6.77 (d,  $J$  = 8.4 Hz, 2H), 6.48 – 6.46 (m, 2H), 6.37 – 6.36 (m, 1H), 4.77 – 4.73 (m, 1H), 4.52 – 4.47 (m, 2H), 3.86 (s, 3H), 3.85 (s, 3H), 3.00 – 2.94 (m, 1H), 2.90 – 2.85 (m, 1H), 2.65 (d,  $J$  = 16.2 Hz, 1H), 2.56 – 2.48 (m, 2H), 2.05 – 2.01 (m, 1H). <sup>13</sup>C NMR (101 MHz, CDCl<sub>3</sub>)  $\delta$  = 155.8, 149.2, 148.2, 143.5, 142.0, 141.5, 141.3, 135.3, 133.3, 129.4, 129.2, 128.85, 128.78, 128.0, 127.7, 127.4, 127.1, 126.6, 125.0, 121.0, 120.5, 120.0, 112.0, 111.6, 66.1, 57.3, 56.1, 49.7, 43.3, 35.1, 30.0, 29.9 ppm (Total count of <sup>13</sup>C is less than

expected due to the merging of signals in the aromatic region). HRMS (ESI) exact mass calculated for  $C_{33}H_{32}N_5O_2^+$  ( $[M+H]^+$ ): 530.2551, found: 530.2553.

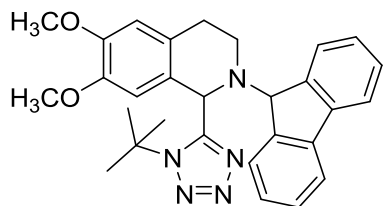
### 1-(1-(cyclohexyl-1H-tetrazol-5-yl)-2-(9H-fluoren-9-yl)-6,7-dimethoxy-1,2,3,4-



**tetrahydroisoquinoline (17r):** According to the general procedure I: 9-fluorenone imine (0.15 mmol, 1.2 equiv, 27 mg), 6,7-dimethoxy-1,2,3,4-tetrahydroisoquinoline hydrochloride (0.38 mmol, 3 equiv, 87 mg), trimethylsilyl azide (0.13 mmol, 1

equiv, 17  $\mu$ L) and triethyl amine (0.19 mmol, 1.5 equiv, 26  $\mu$ L) and Cyclohexyl isocyanide (0.13 mmol, 1 equiv, 16  $\mu$ L) in 2 mL methanol were reacted for 20 hours. After completion of the reaction, the solid product was precipitated from the reaction mixture. Then, the solid was filtered and washed with (3 $\times$ 5 mL) methanol to obtain the desired product **17r** (47 mg) as white solid. Next, mother liquor was evaporated under reduced pressure and residue was purified by column chromatography (Ethyl acetate: hexane; 1:6) to give an additional amount (16 mg) of the product. The combined yield is (63 mg, 96%). FTIR (KBr):  $\tilde{\nu}$  = 3400, 2937, 1609, 1517, 1444, 1248, 1221, 1128, 1010, 747  $cm^{-1}$ .  $^1H$  NMR (400 MHz,  $CDCl_3$ )  $\delta$  = 8.00 (d,  $J$  = 7.6 Hz, 1H), 7.72 – 7.68 (m, 2H), 7.41 – 7.38 (m, 2H), 7.36 – 7.34 (m, 1H), 7.31 – 7.29 (m, 2H), 6.60 (s, 1H), 6.48 (s, 1H), 6.16 (s, 1H), 4.87 – 4.80 (m, 1H), 4.58 (s, 1H), 3.84 (s, 3H), 3.65 (s, 3H), 2.94 – 2.85 (m, 1H), 2.51 – 2.37 (m, 3H), 2.29 – 2.23 (m, 2H), 2.10 – 2.07 (m, 1H), 1.72 – 1.64 (m, 2H), 1.53 – 1.42 (m, 2H), 1.32 – 1.21 (m, 1H), 0.96 – 0.78 (m, 2H) ppm.  $^{13}C$  NMR (151 MHz,  $CDCl_3$ )  $\delta$  = 155.0, 148.7, 148.2, 144.0, 142.2, 141.5, 141.4, 128.8, 128.7, 127.7, 127.6, 127.4, 127.0, 125.1, 124.5, 120.4, 112.0, 111.5, 109.8, 65.9, 58.6, 57.4, 56.22, 56.17, 42.8, 32.9, 32.6, 29.7, 25.9, 25.7, 25.1 ppm. HRMS (ESI) exact mass calculated for  $C_{31}H_{34}N_5O_2^+$  ( $[M+H]^+$ ): 508.2707, found: 508.2709.

### 1-(1-(tert-butyl)-1H-tetrazol-5-yl)-2-(9H-fluoren-9-yl)-6,7-dimethoxy-1,2,3,4-

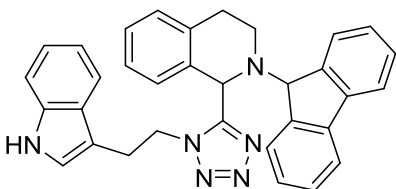


**tetrahydroisoquinoline(17s):** According to general procedure: 9-fluorenone imine (0.15 mmol, 1.2 equiv, 27 mg), 6,7-dimethoxy-1,2,3,4-tetrahydroisoquinoline hydrochloride (0.38 mmol, 3 equiv, 87 mg), trimethylsilyl azide (0.13 mmol, 1 equiv, 17  $\mu$ L)

and triethyl amine (0.19 mmol, 1.5 equiv, 26  $\mu$ L) and *tert*-butyl isocyanide (0.13 mmol, 1 equiv, 16  $\mu$ L) in 2 mL methanol were reacted for 24 hours. After completion of the reaction, the solid product was precipitated from the reaction mixture. Then, the solid was filtered and washed with

(3×5 mL) methanol to obtain the desired product **17s** (26 mg) as white solid. Next, mother liquor was evaporated under reduced pressure and residue was purified by column chromatography (Ethyl acetate: hexane; 1:5) to give an additional amount (16 mg) of the product. The combined yield is (42 mg, 67%). FTIR (KBr):  $\tilde{\nu}$  = 2997, 2835, 1611, 1524, 1471, 1449, 1357, 1260, 1236, 1017, 739, 777  $\text{cm}^{-1}$ .  $^1\text{H}$  NMR (600 MHz,  $\text{CDCl}_3$  at 298 K)  $\delta$  = 8.19 (s, 1H), 7.71 – 7.68 (m, 2H), 7.55 (d,  $J$  = 7.8 Hz, 1H), 7.41 – 7.37 (m, 2H), 7.32 – 7.29 (m, 2H), 6.65 (s, 1H), 6.55 (s, 1H), 5.97 (s, 1H), 4.52 (s, 1H), 3.84 (s, 3H), 3.63 (s, 3H), 2.84 – 2.80 (m, 1H), 2.51 – 2.36 (m, 3H), 1.70 (s, 9H).  $^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ , at 328 K)  $\delta$  8.19 (d,  $J$  = 6.7 Hz, 1H), 7.76 – 7.68 (m, 2H), 7.57 (d,  $J$  = 7.4 Hz, 1H), 7.41 (q,  $J$  = 7.0 Hz, 2H), 7.33 (d,  $J$  = 7.4 Hz, 2H), 6.65 (s, 1H), 6.58 (s, 1H), 6.03 (s, 1H), 4.59 (s, 1H), 3.85 (s, 3H), 3.66 (s, 3H), 2.97 – 2.78 (m, 1H), 2.68 – 2.53 (m, 1H), 2.51 – 2.32 (m, 2H), 1.73 (s, 9H).  $^{13}\text{C}$  NMR (151 MHz,  $\text{CDCl}_3$ )  $\delta$  = 155.1, 148.4, 147.9, 144.0, 141.5, 128.7, 128.6, 127.7, 127.5, 127.4, 126.9, 124.9, 120.2, 119.9, 111.6, 109.0, 66.1, 63.9, 59.5, 56.1, 56.0, 43.1, 30.7, 28.7 ppm. (Total count of  $^{13}\text{C}$  is less than expected due to the merging of signals in the aromatic region.) HRMS (ESI) exact mass calculated for  $\text{C}_{29}\text{H}_{32}\text{N}_5\text{O}_2^+$  ( $[\text{M}+\text{H}]^+$ ): 482.2551, found: 482.2551.

**1-(1-(2-(1H-indol-3-yl)ethyl)-1H-tetrazol-5-yl)-2-(9H-fluoren-9-yl)-1,2,3,4-**

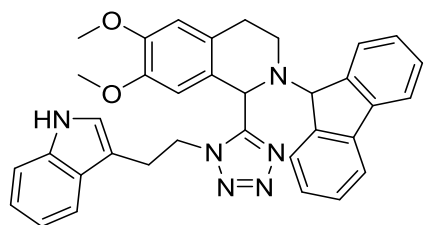


**tetrahydroisoquinoline (17t):** According to the general procedure I: 9-fluorenone imine (0.15 mmol, 1.2 equiv, 27 mg), 1,2,3,4-tetrahydroisoquinoline (0.38 mmol, 3 equiv, 48  $\mu\text{L}$ ), trimethylsilyl azide (0.13 mmol, 1 equiv, 17  $\mu\text{L}$ ) and 3-(2-

isocyanoethyl)-1H-indole (0.13 mmol, 1 equiv, 22 mg) in 2 mL methanol were reacted for 24 hours. After completion of the reaction, the solid product was precipitated from the reaction mixture. Then, the solid was filtered and washed with (3×5 mL) methanol to obtain the desired product **17t** (51 mg) as white solid. Next, mother liquor was evaporated under reduced pressure and residue was purified by column chromatography (Ethyl acetate: hexane; 1:10) to give an additional amount (12 mg) of the product. The combined yield is (63 mg, 96%). FTIR (KBr):  $\tilde{\nu}$  = 3229, 2919, 2860, 1620, 1451, 1361, 1103, 742, 621  $\text{cm}^{-1}$ .  $^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ )  $\delta$  = 8.23 (s, 1H), 7.89 (d,  $J$  = 7.6 Hz, 1H), 7.67 (d,  $J$  = 7.6 Hz, 1H), 7.63 (d,  $J$  = 7.2 Hz, 1H), 7.38 – 7.31 (m, 4H), 7.27 – 7.19 (m, 5H), 7.15 – 7.09 (m, 3H), 6.78 (s, 1H), 6.74 (d,  $J$  = 7.6 Hz, 1H), 6.45 (s, 1H), 4.80 – 4.73 (m, 1H), 4.66 – 4.59 (m, 1H), 4.50 (s, 1H), 3.21 – 3.13 (m, 1H), 2.95 – 2.89 (m, 1H), 2.61 – 2.57 (m, 1H), 2.53 – 2.39 (m, 3H).  $^{13}\text{C}$  NMR (151 MHz,  $\text{CDCl}_3$ )  $\delta$  = 155.7, 143.4,

141.9, 141.3, 141.0, 136.2, 135.1, 133.0, 129.4, 128.6, 127.8, 127.6, 127.3, 127.1, 126.9, 126.8, 126.5, 124.9, 122.6, 122.3, 120.4, 120.3, 119.7, 119.6, 118.4, 111.4, 110.9, 66.0, 57.2, 48.7, 43.0, 29.7, 25.0 ppm. HRMS (ESI) exact mass calculated for  $C_{33}H_{29}N_6^+$  ( $[M+H]^+$ ): 509.2448, found: 509.2448.

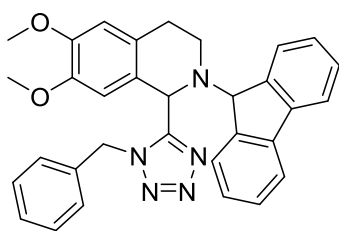
**1-(1-(2-(1H-indol-3-yl)ethyl)-1H-tetrazol-5-yl)-2-(9H-fluoren-9-yl)-6,7-dimethoxy-1,2,3,4-**



**tetrahydroisoquinoline (17u):** According to the general procedure I: 9-fluorenone imine (0.15 mmol, 1.2 equiv, 27 mg), 6,7-dimethoxy-1,2,3,4-tetrahydroisoquinoline hydrochloride (0.38 mmol, 3 equiv, 87 mg), trimethylsilyl azide (0.13 mmol, 1 equiv, 17  $\mu$ L) and triethyl amine (0.19

mmol, 1.5 equiv, 26  $\mu$ L) and 3-(2-isocyanoethyl)-1H-indole (0.13 mmol, 1 equiv, 22 mg) in 2 mL methanol were reacted for 16 hours. After completion of the reaction, the solid product was precipitated from the reaction mixture. Then, the solid was filtered and washed with (3 $\times$ 5 mL) methanol to obtain the desired product **17u** (51 mg) as white solid. Next, mother liquor was evaporated under reduced pressure and residue was purified by column chromatography (Ethyl acetate: hexane; 1:4) to give an additional amount (12 mg) of the product. The combined yield is (63 mg, 85%). FTIR (KBr):  $\tilde{\nu}$  = 3412, 3069, 2959, 2824, 1958, 1603, 1655, 1589, 1521, 1447, 1294, 1247, 1124, 1084, 1024, 746, 520  $cm^{-1}$ .  $^1H$  NMR (600 MHz,  $CDCl_3$ )  $\delta$  = 8.06 (s, 1H), 7.89 (d,  $J$  = 7.2 Hz, 1H), 7.69 (d,  $J$  = 7.8 Hz, 1H), 7.65 (d,  $J$  = 7.8 Hz, 1H), 7.40 – 7.37 (m, 4H), 7.28 – 7.19 (m, 2H), 7.17 – 7.15 (m, 1H), 7.11 – 7.10 (m, 1H), 6.83 (d,  $J$  = 1.8 Hz, 1H), 6.59 (s, 1H), 6.40 (s, 1H), 6.17 (s, 1H), 4.89 – 4.83 (m, 1H), 4.72 – 4.66 (m, 1H), 4.54 (s, 1H), 3.82 (s, 3H), 3.63 (s, 3H), 3.25 – 3.18 (m, 1H), 2.89 – 2.84 (m, 1H), 2.72 – 2.66 (m, 1H), 2.49 – 2.46 (m, 3H).  $^{13}C$  NMR (50 MHz,  $CDCl_3$ )  $\delta$  = 156.0, 148.8, 148.2, 143.6, 142.1, 141.5, 141.2, 136.3, 128.7, 127.7, 127.5, 127.3, 127.1, 126.6, 125.0, 124.6, 122.5, 120.4, 119.9, 119.7, 118.5, 111.6, 111.2, 109.7, 66.2, 57.1, 56.2, 56.1, 48.9, 43.3, 29.5, 25.1 ppm. (Total count of  $^{13}C$  is less than expected due to the merging of signals in the aromatic region.) HRMS (ESI) exact mass calculated for  $C_{35}H_{33}N_6^+$  ( $[M+H]^+$ ): 569.2660, found: 569.2660.

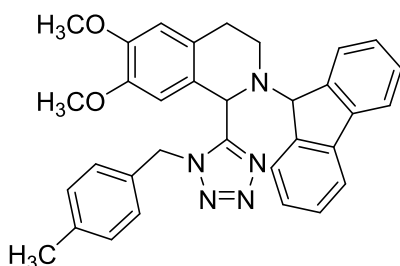
### 1-(1-benzyl-1H-tetrazol-5-yl)-2-(9H-fluoren-9-yl)-6,7-dimethoxy-1,2,3,4-



**tetrahydroisoquinoline (17v):** According to the general procedure I:

9-fluorenone imine (0.24 mmol, 1.2 equiv, 43 mg), 6,7-dimethoxy-1,2,3,4-tetrahydroisoquinoline hydrochloride (0.6 mmol, 3 equiv, 137 mg), trimethylsilyl azide (0.2 mmol, 1 equiv, 26  $\mu$ L) and triethyl amine (0.3 mmol, 1.5 equiv, 41  $\mu$ L) and benzyl isocyanide (0.2 mmol, 1 equiv, 24 mg) in 2 mL methanol were reacted for 24 hours. After completion of the reaction, the solid product was precipitated from the reaction mixture. Then, the solid was filtered and washed with (3 $\times$ 5 mL) methanol to obtain the desired product (70 mg) as white solid. Next, mother liquor was evaporated under reduced pressure and residue was purified by column chromatography (Ethyl acetate: hexane; 1:5) to give an additional amount (10 mg) of the product. The combined yield is (80 mg, 78%). FTIR (KBr):  $\tilde{\nu}$  = 3420, 2875, 1609, 1519, 1450, 1255, 1213, 1133, 847, 736, 721, 702  $\text{cm}^{-1}$ .  $^1\text{H}$  NMR (600 MHz,  $\text{CDCl}_3$ )  $\delta$  = 7.87 (d,  $J$  = 6.0 Hz, 1H), 7.72 – 7.69 (m, 2H), 7.42 – 7.37 (m, 2H), 7.29 – 7.25 (m, 3H), 7.21 – 7.18 (m, 1H), 7.13 – 7.11 (m, 2H), 6.79 – 6.77 (m, 2H), 6.49 (s, 1H), 6.30 (s, 1H), 5.81 – 5.79 (m, 2H), 5.52 – 5.49 (m, 1H), 4.59 (s, 1H), 3.80 (s, 3H), 3.38 (s, 3H), 2.96 – 2.91 (m, 1H), 2.67 – 2.54 (m, 3H).  $^{13}\text{C}$  NMR (151 MHz,  $\text{CDCl}_3$ )  $\delta$  = 155.9, 148.7, 147.9, 143.7, 142.2, 141.4, 141.3, 133.3, 128.9, 128.8, 128.6, 128.4, 127.73, 127.70, 127.4, 127.1, 126.7, 125.1, 124.4, 120.4, 120.0, 111.5, 109.6, 66.5, 56.6, 56.0, 55.8, 51.4, 43.6, 29.6 ppm. HRMS (ESI) exact mass calculated for  $\text{C}_{32}\text{H}_{30}\text{N}_2\text{O}_5^+$  ( $[\text{M}+\text{H}]^+$ ): 516.2394, found: 516.2393.

### 2-(9H-fluoren-9-yl)-6,7-dimethoxy-1-(1-(4-methylbenzyl)-1H-tetrazol-5-yl)-1,2,3,4-

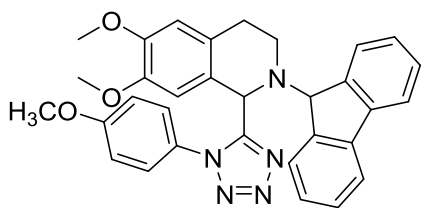


**tetrahydroisoquinoline (17w):** According to the general procedure I: 9-fluorenone imine (0.15 mmol, 1.2 equiv, 27 mg), 6,7-dimethoxy-1,2,3,4-tetrahydroisoquinoline hydrochloride (0.38 mmol, 3 equiv, 87 mg), trimethylsilyl azide (0.13 mmol, 1 equiv, 17  $\mu$ L) and triethyl amine (0.19 mmol, 1.5 equiv, 26  $\mu$ L)

and *para*-methyl benzyl isocyanide (0.13 mmol, 1 equiv, 17 mg) in 2 mL methanol were reacted for 24 hours. After completion of the reaction, the solid product was precipitated from the reaction mixture. Then, the solid was filtered and washed with (3 $\times$ 5 mL) methanol to obtain the desired product **17w** (47 mg) as white solid. Next, mother liquor was evaporated under reduced pressure and residue was purified by column chromatography (Ethyl acetate: hexane; 1:6) to obtain an

additional amount (16 mg) of the product. The combined yield is (63 mg, 96%). FTIR (KBr):  $\tilde{\nu}$  = 3024, 2938, 2917, 2830, 1614, 1520, 1450, 1252, 1219, 1129, 1015, 786, 747, 674, 476  $\text{cm}^{-1}$ .  $^1\text{H}$  NMR (600 MHz,  $\text{CDCl}_3$ )  $\delta$  = 7.85 (d,  $J$  = 6.6 Hz, 1H), 7.70 – 7.67 (m, 2H), 7.40 – 7.35 (m, 2H), 7.28 – 7.24 (m, 3H), 6.93 (d,  $J$  = 7.8 Hz, 2H), 6.66 (d,  $J$  = 7.8 Hz, 2H), 6.51 (s, 1H), 6.27 (s, 1H), 5.81 (s, 1H), 5.72 (d,  $J$  = 15.0 Hz, 1H), 5.41 – 5.39 (m, 1H), 4.57 (s, 1H), 3.81 (s, 3H), 3.40 (s, 3H), 2.94 – 2.90 (m, 1H), 2.65 – 2.54 (m, 3H), 2.26 (s, 3H).  $^{13}\text{C}$  NMR (151 MHz,  $\text{CDCl}_3$ )  $\delta$  = 155.8, 148.7, 148.0, 143.6, 142.2, 141.3, 141.2, 138.2, 130.4, 129.3, 128.8, 128.7, 127.8, 127.6, 127.3, 127.1, 126.6, 125.1, 124.5, 120.4, 119.9, 111.5, 109.7, 66.5, 56.6, 56.0, 55.8, 51.3, 43.7, 29.5, 21.2 ppm. HRMS (ESI) exact mass calculated for  $\text{C}_{33}\text{H}_{32}\text{N}_5\text{O}_2^+$  ( $[\text{M}+\text{H}]^+$ ): 530.2551, found: 530.2551.

**2-(9H-fluoren-9-yl)-6,7-dimethoxy-1-(1-(4-methoxyphenyl)-1H-tetrazol-5-yl)-1,2,3,4-**

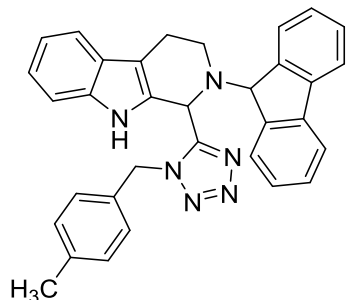


**tetrahydroisoquinoline (17x):** According to the general procedure I: 9-fluorenone imine (0.15 mmol, 1.2 equiv, 27 mg), 6,7-dimethoxy-1,2,3,4-tetrahydroisoquinoline hydrochloride (0.38 mmol, 3 equiv, 87 mg), triethyl amine

(0.19 mmol, 1.5 equiv, 26  $\mu\text{L}$ ) and *para*-methoxy phenyl isocyanide (0.13 mmol, 1 equiv, 17 mg) in 2 mL methanol were reacted for 24 hours. After completion of the reaction, the solid product was precipitated from the reaction mixture. Then, the solid was filtered and washed with (3 $\times$ 5 mL) methanol to get the desired product **17x** (42 mg) as white solid. Next, mother liquor was evaporated under reduced pressure and residue was purified by column chromatography (Ethyl acetate: hexane; 1:6) to give an additional amount (11 mg) of the product. The combined yield is (53 mg, 77%). FTIR (KBr):  $\tilde{\nu}$  = 3059, 3006, 2939, 2913, 2840, 1878, 1609, 1590, 1404, 1300, 1220, 1198, 1011, 980, 846, 734, 621, 535  $\text{cm}^{-1}$ .  $^1\text{H}$  NMR (600 MHz,  $\text{CDCl}_3$ )  $\delta$  = 7.88 (d,  $J$  = 7.8 Hz, 1H), 7.68 (d,  $J$  = 7.2 Hz, 1H), 7.62 (d,  $J$  = 7.2 Hz, 1H), 7.37 – 7.32 (m, 2H), 7.27 – 7.24 (m, 1H), 7.17 – 7.15 (m, 3H), 6.87 (d,  $J$  = 9.0 Hz, 2H), 6.81 (d,  $J$  = 7.2 Hz, 1H), 6.49 (s, 1H), 6.47 (s, 1H), 6.31 (s, 1H), 4.62 (s, 1H), 3.86 (s, 3H), 3.82 (s, 3H), 3.70 (s, 3H), 2.49 – 2.44 (m, 1H), 2.38 – 2.36 (m, 2H), 2.30 – 2.27 (m, 1H).  $^{13}\text{C}$  NMR (151 MHz,  $\text{CDCl}_3$ )  $\delta$  = 160.7, 156.2, 148.5, 148.0, 143.8, 142.3, 141.4, 141.0, 128.6, 128.5, 128.1, 127.9, 127.5, 127.3, 127.0, 126.8, 125.14, 125.07, 120.3, 119.7,

114.0, 111.4, 109.3, 66.0, 57.4, 56.2, 56.1, 55.9, 42.8, 29.1 ppm. HRMS (ESI) exact mass calculated for  $C_{32}H_{30}N_5O_3^+$  ( $[M+H]^+$ ): 532.2343, found: 532.2338.

**2-(9H-fluoren-9-yl)-1-(1-(4-methylbenzyl)-1H-tetrazol-5-yl)-2,3,4,9-tetrahydro-1H-**



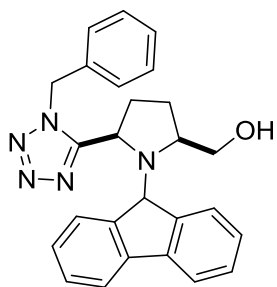
**pyrido[3,4-b]indole (17y):** According to the general procedure I: 9-fluorenone imine (0.15 mmol, 1.2 equiv, 27 mg), 2,3,4,9-tetrahydro-1H-pyrido[3,4-b]indole (0.38 mmol, 3 equiv, 22 mg), trimethylsilyl azide (0.13 mmol, 1 equiv, 17  $\mu$ L) and *para*-methyl benzyl isocyanide (0.13 mmol, 1 equiv, 18 mg) in 2 mL methanol were reacted for 36 hours. The crude product was purified by  $SiO_2$  column chromatography (ethyl acetate: hexane; 1:6) to obtain **17y** as brown solid (22 mg, 33%).

FTIR (KBr):  $\tilde{\nu}$  = 2997, 2835, 1611, 1524, 1471, 1449, 1357, 1260, 1236, 1017, 739, 777  $cm^{-1}$ .  $^1H$  NMR (600 MHz,  $CDCl_3$ )  $\delta$  7.81 (d,  $J$  = 7.2 Hz, 1H), 7.71 – 7.70 (m, 2H), 7.53 – 7.49 (m, 1H), 7.44 – 7.32 (m, 2H), 7.40 – 7.36 (m, 1H), 7.29 – 7.28 (m, 2H), 7.25 – 7.22 (m, 1H), 7.11 – 7.06 (m, 2H), 7.01 (d,  $J$  = 7.8 Hz, 1H), 6.66 (d,  $J$  = 7.8 Hz, 2H), 6.56 (d,  $J$  = 7.8 Hz, 2H), 6.39 (s, 1H), 5.86 (d,  $J$  = 14.4 Hz, 1H), 5.41 – 5.39 (m, 1H), 4.69 (s, 1H), 2.85 – 2.83 (m, 3H), 2.71 – 2.69 (m, 1H), 2.10 (s, 3H).  $^{13}C$  NMR (151 MHz,  $CDCl_3$ )  $\delta$  = 154.0, 143.7, 142.3, 141.3, 141.2, 138.4, 136.7, 130.0, 129.2, 128.9, 128.8, 128.7, 127.7, 127.7, 127.4, 126.5, 126.5, 125.3, 122.6, 120.5, 120.0, 119.9, 118.6, 111.5, 111.0, 66.5, 51.6, 44.7, 29.9, 22.2, 21.2 ppm. HRMS (ESI) exact mass calculated for  $C_{33}H_{29}N_6^+$  ( $[M+H]^+$ ): 509.2448, found: 509.2442.

**General procedure II:** Isocyanides derivatives (0.13 mmol, 1 equiv), trimethylsilyl azide (0.13 mmol, 1 equiv), imine (0.15 mmol, 1.2 equiv), *N* heterocycles (0.38 mmol, 3 equiv) and acetic acid (0.13 mmol, 1 equiv) were taken in closed tube in neat condition and the mixture was stirred at 100  $^{\circ}C$  (oil bath temperature) for 12 hours. The residue was purified by column chromatography to obtain analytically pure  $\alpha$ - tetrazoyl *N* heterocycles.

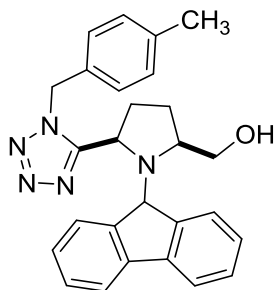


**((2S,5R)-5-(1-benzyl-1H-tetrazol-5-yl)-1-(9H-fluoren-9-yl)pyrrolidin-2-yl)methanol (19a):**



According to the general procedure II : 9-fluorenone imine (0.15 mmol, 1.2 equiv, 27 mg), (*S*)-pyrrolidin-2-ylmethanol (0.38 mmol, 3 equiv, 37  $\mu$ L), trimethylsilyl azide (0.13 mmol, 1 equiv, 17  $\mu$ L) and benzyl isocyanide (0.13 mmol, 1 equiv, 15 mg ) and acetic acid (0.13 mmol, 1 equiv, 7  $\mu$ L) were reacted for 12 hours. The crude product was purified by SiO<sub>2</sub> column chromatography (ethyl acetate: hexane; 1:1) to obtain **19a** as brown a solid compound (30 mg, 54%). FTIR (KBr):  $\tilde{\nu}$  = 3062, 2925, 1650, 1631, 1449, 1403, 1086, 1008, 743 cm<sup>-1</sup>.  $[\alpha]_D^{25}$  = - 23.33 (c = 0.12, MeOH). <sup>1</sup>H NMR (600 MHz, CDCl<sub>3</sub>)  $\delta$  = 7.79 (d, *J* = 7.8 Hz, 1H), 7.65 (d, *J* = 7.2 Hz, 2H), 7.51 – 7.47 (m, 1H), 7.37 – 7.34 (m, 1H), 7.29 – 7.28 (m, 1H), 7.21 – 7.18 (m, 1H), 7.16 – 7.13 (m, 3H), 7.06 – 7.04 (m, 1H), 6.61 (d, *J* = 7.8 Hz, 1H), 5.12 (s, 1H), 5.05 (d, *J* = 15.6 Hz, 1H), 4.17 (d, *J* = 15.0 Hz, 1H), 4.04 – 4.02 (m, 2H), 3.73 – 3.68 (m, 1H), 3.61 – 3.57 (m, 1H), 2.33 – 2.27 (m, 1H), 2.01 – 1.96 (m, 1H), 1.63 – 1.55 (m, 2H). <sup>13</sup>C NMR (151 MHz, CDCl<sub>3</sub>)  $\delta$  = 159.8, 143.9, 143.7, 141.7, 139.7, 133.4, 129.2, 129.1, 128.8, 128.7, 127.8, 127.3, 126.2, 125.6, 120.4, 119.7, 65.2, 65.0, 63.2, 52.4, 50.2, 32.5, 27.2 ppm. HRMS (ESI) exact mass calculated for C<sub>26</sub>H<sub>26</sub>N<sub>5</sub>O<sup>+</sup> ([M+H]<sup>+</sup>): 424.2132, found: 424.2134. The enantiomeric excess (>99 %) was determined by HPLC analysis; column: phenomenex lux 5u cellulose -1; solvent: 2-propanol: hexane (12:88); uv light: 254 nm; flow: 1 mL /min; major enantiomer *t<sub>r</sub>* = 42.26 min, minor enantiomer *t<sub>r</sub>* = 38.82 min.

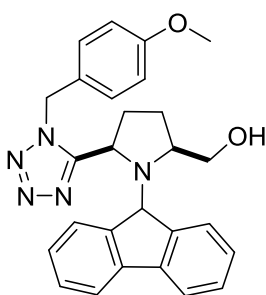
**((2S,5R)-1-(9H-fluoren-9-yl)-5-(1-(4-methylbenzyl)-1H-tetrazol-5-yl)pyrrolidin-2-yl)methanol (19b):**



According to the general procedure II : 9-fluorenone imine (0.15 mmol, 1.2 equiv, 27 mg), (*S*)-pyrrolidin-2-ylmethanol (0.38 mmol, 3 equiv, 37  $\mu$ L), trimethylsilyl azide (0.13 mmol, 1 equiv, 17  $\mu$ L) and *para*-methyl benzyl isocyanide (0.13 mmol, 1 equiv, 17 mg ) and acetic acid (0.13 mmol, 1 equiv, 7  $\mu$ L) were reacted for 12 hours. The crude product was purified by SiO<sub>2</sub> column chromatography (ethyl acetate: hexane; 1:1) to obtain **19b** as brown compound (34 mg, 60%) FTIR (KBr):  $\tilde{\nu}$  = 3419, 2924, 2874, 1446, 1433, 1080, 745 cm<sup>-1</sup>.  $[\alpha]_D^{25}$  = -11.82 (c = 0.22, MeOH). <sup>1</sup>H NMR (600 MHz, CDCl<sub>3</sub>)  $\delta$  = 7.78 (d, *J* = 7.2 Hz, 1H), 7.66 – 7.62 (m, 2H), 7.50 – 7.48 (m, 1H), 7.36 – 7.34 (m, 1H), 7.28 – 7.25 (m, 1H), 7.15 – 7.14 (m, 1H), 7.05 – 7.02 (m, 1H), 6.92 (d, *J* = 8.4 Hz, 2H), 6.51 (d, *J* = 7.8 Hz, 2H), 5.10 (s, 1H), 4.99 (d, *J* = 15.6 Hz, 1H), 4.17 (d, *J* = 15.0 Hz, 1H), 4.01 – 4.00 (m, 2H),

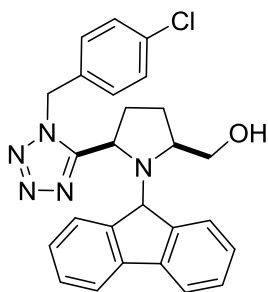
3.70 – 3.68 (m, 1H), 3.64 – 3.60 (m, 1H), 2.32 – 2.27 (m, 1H), 2.25 (s, 3H), 2.02 – 1.96 (m, 1H), 1.66 – 1.55 (m, 2H).  $^{13}\text{C}$  NMR (151 MHz,  $\text{CDCl}_3$ )  $\delta$  = 159.7, 144.0, 143.8, 141.7, 139.7, 138.7, 130.4, 129.8, 129.0, 128.6, 127.8, 127.7, 127.3, 126.2, 125.6, 120.3, 119.7, 65.1, 65.0, 63.3, 52.6, 50.1, 32.5, 27.2, 21.3 ppm. HRMS (ESI) exact mass calculated for  $\text{C}_{27}\text{H}_{28}\text{N}_5\text{O}^+$  ( $[\text{M}+\text{H}]^+$ ): 438.2288, found: 438.2293 The enantiomeric excess (>96 %) was determined by HPLC analysis; column: phenomenex lux 5u cellulose -1; solvent: 2-propanol: hexane (15:85); UV light: 254 nm; flow: 1 mL /min; major enantiomer  $t_r$  = 28.58 min, minor enantiomer  $t_r$  = 25.46 min.

**((2S,5R)-1-(9H-fluoren-9-yl)-5-(1-(4-methoxybenzyl)-1H-tetrazol-5-yl)pyrrolidin-2-**



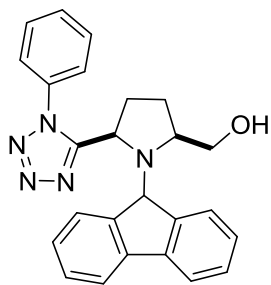
**yl)methanol (19c):** According to the general procedure II : 9-fluorenone imine (0.15 mmol, 1.2 equiv, 27 mg), (*S*)-pyrrolidin-2-ylmethanol (0.38 mmol, 3 equiv, 37  $\mu\text{L}$ ), trimethylsilyl azide (0.13 mmol, 1 equiv, 17  $\mu\text{L}$ ) and *para*-methoxy benzyl isocyanide (0.13 mmol, 1 equiv, 19 mg) and acetic acid (0.13 mmol, 1 equiv, 7  $\mu\text{L}$ ) in neat condition were reacted for 12 hours. The crude product was purified by  $\text{SiO}_2$  column chromatography (ethyl acetate: hexane; 1:1) to obtain **19c** as brown compound (38 mg, 64%). FTIR (KBr):  $\tilde{\nu}$  = 2923, 2852, 1638, 1452, 1260, 1025, 804, 749  $\text{cm}^{-1}$ .  $[\alpha]_D^{25} = -18.52$  ( $c = 0.27$ , MeOH).  $^1\text{H}$  NMR (600 MHz,  $\text{CDCl}_3$ )  $\delta$  = 7.78 (d,  $J = 7.8$  Hz, 1H), 7.66 (d,  $J = 7.8$  Hz, 1H), 7.63 (d,  $J = 7.8$  Hz, 1H), 7.51 – 7.48 (m, 1H), 7.37 – 7.34 (m, 1H), 7.28 – 7.27 (m, 1H), 7.15 (d,  $J = 7.2$  Hz, 1H), 7.05 – 7.03 (m, 1H), 6.63 – 6.62 (m, 2H), 6.55 (m, 2H), 5.11 (s, 1H), 4.96 (d,  $J = 15.0$  Hz, 1H), 4.16 (d,  $J = 15.0$  Hz, 1H), 4.05 – 4.02 (m, 2H), 3.73 (s, 3H), 3.71 – 3.70 (m, 1H), 3.64 – 3.56 (m, 1H), 2.34 – 2.28 (m, 1H), 2.03 – 1.96 (m, 1H), 1.67 – 1.63 (m, 1H), 1.58 – 1.55 (m, 1H).  $^{13}\text{C}$  NMR (151 MHz,  $\text{CDCl}_3$ )  $\delta$  = 159.8, 159.7, 144.0, 143.8, 141.7, 139.6, 129.0, 128.9, 128.7, 127.8, 126.3, 125.6, 125.3, 120.3, 119.7, 114.5, 65.2, 64.9, 63.1, 55.4, 52.5, 49.9, 32.5, 27.1 ppm. HRMS (ESI) exact mass calculated for  $\text{C}_{27}\text{H}_{28}\text{N}_5\text{O}_2^+$  ( $[\text{M}+\text{H}]^+$ ): 454.2238, found: 454.2243. (Total count of  $^{13}\text{C}$  is less than expected due to the merging of signals in the aromatic region). HPLC analysis: column: phenomenex lux 5u cellulose -1; solvent: 2-propanol: hexane (20:80); UV light: 291 nm; flow: 1 mL /min; major enantiomer  $t_r$  = 27.85 min, minor enantiomer  $t_r$  = 22.17 min.

**((2S,5R)-5-(1-(4-chlorobenzyl)-1H-tetrazol-5-yl)-1-(9H-fluoren-9-yl)pyrrolidin-2-yl)methanol (19d):**



**yl)methanol (19d):** According to the general procedure II : 9-fluorenone imine (0.15 mmol, 1.2 equiv, 27 mg), (*S*)-pyrrolidin-2-ylmethanol (0.38 mmol, 3 equiv, 37  $\mu$ L), trimethylsilyl azide (0.13 mmol, 1 equiv, 17  $\mu$ L) and *para*-chloro benzyl isocyanide (0.13 mmol, 1 equiv, 20 mg) and acetic acid (0.13 mmol, 1 equiv, 7  $\mu$ L) in neat condition were reacted for 12 hours. The crude product was purified by SiO<sub>2</sub> column chromatography (ethyl acetate: hexane; 1:1) to obtain **19d** as brown compound (32 mg, 54%). FTIR (KBr):  $\tilde{\nu}$ = 2922, 2853, 1638, 1492, 1448, 1410, 1083, 1014, 802, 747 cm<sup>-1</sup>.  $[\alpha]_D^{25}$  = - 81.33 (c = 0.15, MeOH) <sup>1</sup>H NMR (600 MHz, CDCl<sub>3</sub>)  $\delta$  = 7.77 (d, *J* = 7.8 Hz, 1H), 7.65 (d, *J* = 7.2 Hz, 1H), 7.61 (d, *J* = 7.2 Hz, 1H), 7.51 – 7.48 (m, 1H), 7.36 – 7.34 (m, 1H), 7.29 – 7.24 (m, 1H), 7.19 – 7.17 (m, 1H), 7.09 – 7.08 (m, 2H), 7.04 – 7.02 (m, 1H), 6.52 (d, *J* = 8.4 Hz, 2H), 5.12 (s, 1H), 4.93 (d, *J* = 15.6 Hz, 1H), 4.35 (d, *J* = 15.6 Hz, 1H), 4.08 – 4.07 (m, 2H), 3.74 (d, *J* = 9.6 Hz, 1H), 3.56 – 3.49 (m, 1H), 2.35 – 2.29 (m, 1H), 2.06 – 2.02 (m, 1H), 1.77 – 1.75 (m, 1H), 1.65 – 1.60 (m, 1H). <sup>13</sup>C NMR (151 MHz, CDCl<sub>3</sub>)  $\delta$ = 159.7, 143.8, 143.7, 141.7, 139.5, 134.8, 131.7, 129.5, 129.1, 128.64, 128.61, 127.8, 126.3, 125.5, 120.4, 119.7, 65.4, 64.9, 62.9, 52.3, 49.5, 32.6, 26.9. HRMS (ESI) exact mass calculated for C<sub>26</sub>H<sub>25</sub>ClN<sub>5</sub>O<sup>+</sup> ([M+H]<sup>+</sup>): 458.1742, found: 458.1753. HPLC analysis: column: phenomenex lux 5u cellulose -1; solvent: 2-propanol: hexane (25:75); UV light: 254 nm; flow: 1 mL/min; major enantiomer *t*<sub>r</sub> = 31.30 min, minor enantiomer *t*<sub>r</sub> = 15.48 min.

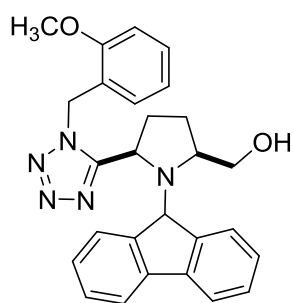
**((2S,5R)-1-(9H-fluoren-9-yl)-5-(1-phenyl-1H-tetrazol-5-yl)pyrrolidin-2-yl)methanol (19e):**



According to the general procedure II : 9-fluorenone imine (0.15 mmol, 1.2 equiv, 27 mg), (*S*)-pyrrolidin-2-ylmethanol (0.38 mmol, 3 equiv, 37  $\mu$ L), trimethylsilyl azide (0.13 mmol, 1 equiv, 17  $\mu$ L) and phenyl isocyanide (0.13 mmol, 1 equiv, 13 mg) and acetic acid (0.13 mmol, 1 equiv, 7  $\mu$ L) in neat condition were reacted for 12 hours. The crude product was purified by SiO<sub>2</sub> column chromatography (ethyl acetate: hexane; 1:1) to obtain **19e** as brown compound (27 mg, 51%) FTIR (KBr):  $\tilde{\nu}$ = 2923, 2852, 1742, 1450, 1261, 1084, 744 cm<sup>-1</sup>.  $[\alpha]_D^{25}$  = - 5.26 (c = 0.38, MeOH) <sup>1</sup>H NMR (600 MHz, CDCl<sub>3</sub>)  $\delta$  = 7.61 (d, *J* = 7.2 Hz, 1H), 7.54 (d, *J* = 7.8 Hz, 2H), 7.39 (t, *J* = 7.5 Hz, 1H), 7.40 – 7.38 (m, 1H), 7.34 – 7.31 (m, 3H), 7.25 – 7.21 (m, 2H), 7.08 – 7.06 (m, 1H), 6.55 (d, *J* = 7.2 Hz, 2H), 5.12 (s, 1H), 4.12 – 4.09 (m, 2H), 3.78 – 3.76 (m, 1H), 3.68 – 3.67 (m, 1H), 2.54 – 2.48 (m, 1H), 2.12 –

2.08 (m, 1H), 2.00 – 1.96 (m, 1H), 1.84 – 1.79 (m, 1H).  $^{13}\text{C}$  NMR (151 MHz,  $\text{CDCl}_3$ )  $\delta$  = 160.5, 143.8, 143.7, 141.5, 140.0, 132.9, 130.4, 129.5, 128.8, 128.6, 127.7, 127.6, 126.3, 125.4, 125.1, 120.0, 119.7, 65.2, 64.6, 62.7, 52.6, 33.3, 26.9 ppm. HRMS (ESI) exact mass calculated for  $\text{C}_{25}\text{H}_{24}\text{N}_5\text{O}^+$  ( $[\text{M}+\text{H}]^+$ ): 410.1975, found: 410.1995. HPLC analysis: column: phenomenex lux 5u cellulose -1; solvent: 2-propanol: hexane (1:5); UVlight: 291 nm; flow: 1 mL /min; major enantiomer  $t_r$  = 24.02 min, minor enantiomer  $t_r$  = 20.25 min.

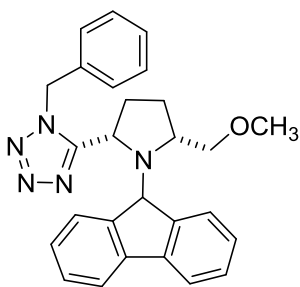
**((2S,5R)-1-(9H-fluoren-9-yl)-5-(1-(2-methoxybenzyl)-1H-tetrazol-5-yl)pyrrolidin-2-**



**yl)methanol (19f):** According to the general procedure II : 9-fluorenone imine (0.15 mmol, 1.2 equiv, 27 mg), (*S*)-pyrrolidin-2-ylmethanol (0.38 mmol, 3 equiv, 37  $\mu\text{L}$ ), trimethylsilyl azide (0.13 mmol, 1 equiv, 17  $\mu\text{L}$ ) and *ortho*-methoxy benzyl isocyanide (0.13 mmol, 1 equiv, 19 mg) and acetic acid (0.13 mmol, 1 equiv, 7  $\mu\text{L}$ ) in neat condition were reacted for 12 hours. The crude product was purified by  $\text{SiO}_2$  column

chromatography (ethyl acetate: hexane; 1:1) to obtain **19f** as brown compound (30 mg, 51%). FTIR (KBr):  $\tilde{\nu}$  = 2923, 2853, 1637, 1495, 1449, 1251, 1082, 1025, 745  $\text{cm}^{-1}$ .  $[\alpha]_D^{25} = -6.00$  ( $c = 0.50$ )  $^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ )  $\delta$  = 7.76 (d,  $J = 7.6$  Hz, 1H), 7.69 (d,  $J = 7.6$  Hz, 1H), 7.63 (d,  $J = 7.6$  Hz, 1H), 7.49 – 7.45 (m, 1H), 7.36 – 7.32 (m, 1H), 7.29 – 7.27 (m, 1H), 7.20 – 7.13 (m, 2H), 7.04 – 7.02 (m, 1H), 6.73– 6.63 (m, 3H), 5.12 (s, 1H), 4.83 (d,  $J = 15.2$  Hz, 1H), 4.45 (d,  $J = 15.2$  Hz, 1H), 4.04 – 4.02 (m, 2H), 3.80 – 3.75 (m, 1H), 3.71 – 3.69 (m, 1H), 3.46 (s, 3H), 2.39 – 2.29 (m, 1H), 2.04 – 1.96 (m, 1H), 1.79 – 1.71 (m, 1H), 1.59 – 1.56 (m, 1H).  $^{13}\text{C}$  NMR (151 MHz,  $\text{CDCl}_3$ )  $\delta$  = 159.9, 156.4, 144.3, 143.8, 141.8, 139.8, 130.4, 129.8, 128.9, 128.6, 127.7, 127.6, 126.2, 125.6, 121.5, 121.0, 120.4, 119.8, 110.6, 65.0, 64.9, 63.0, 55.2, 44.8, 32.5, 27.1 ppm. HRMS (ESI) exact mass calculated for  $\text{C}_{27}\text{H}_{28}\text{N}_5\text{O}_2^+$  ( $[\text{M}+\text{H}]^+$ ): 454.2238, found: 454.2272. HPLC column: phenomenex lux 5u cellulose -1; solvent: 2-propanol: hexane (7:93); UV light: 291 nm; flow: 1 mL /min; major enantiomer  $t_r$  = 94.49 min, minor enantiomer  $t_r$  = 86.82 min.

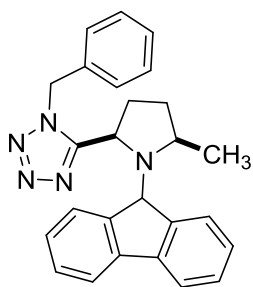
### 5-((2*S*,5*R*)-1-(9*H*-fluoren-9-yl)-5-(methoxymethyl)pyrrolidin-2-yl)-1-benzyl-1*H*-



**tetrazole(19g):** According to the general procedure II : 9-fluorenone imine (0.15 mmol, 1.2 equiv, 27 mg), (*R*)-2-(methoxymethyl)pyrrolidine (0.38 mmol, 3 equiv, 47  $\mu$ L), trimethylsilyl azide (0.13 mmol, 1 equiv, 17  $\mu$ L) and benzyl isocyanide (0.13 mmol, 1 equiv, 15 mg) and acetic acid (0.13 mmol, 1 equiv, 7  $\mu$ L) in neat condition were reacted for 12 hours. The crude product was purified by

SiO<sub>2</sub> column chromatography (ethyl acetate: hexane; 1:1) to obtain **19g** as brown compound (35 mg, 53%) FTIR (KBr):  $\tilde{\nu}$  = 2925, 2853, 1452, 1261, 1091, 1025, 804, 749, 720 cm<sup>-1</sup>.  $[\alpha]_D^{25}$  = -40.00 (*c* = 0.28, MeOH). <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>)  $\delta$  = 7.80 (d, *J* = 7.6 Hz, 1H), 7.68 – 7.62 (m, 2H), 7.50 – 7.46 (m, 1H), 7.36 – 7.28 (m, 3H), 7.20 – 7.14 (m, 3H), 7.11 – 7.07 (m, 1H), 6.70 (d, *J* = 6.8 Hz, 2H), 5.34 (d, *J* = 15.6 Hz, 1H), 5.26 (s, 1H), 4.22 (d, *J* = 15.6 Hz, 1H), 3.93 – 3.84 (m, 2H), 3.66 – 3.63 (m, 1H), 3.55 – 3.51 (m, 1H), 3.41 (s, 3H), 2.08 – 2.02 (m, 2H), 1.74 – 1.67 (m, 2H). <sup>13</sup>C NMR (151 MHz, CDCl<sub>3</sub>)  $\delta$  = 158.1, 144.3, 144.2, 141.5, 139.8, 134.3, 129.1, 128.9, 128.7, 128.5, 127.7, 127.6, 127.2, 126.0, 125.9, 120.4, 119.8, 77.6, 66.0, 63.0, 59.4, 53.3, 50.0, 31.7, 28.9. HRMS (ESI) exact mass calculated for C<sub>27</sub>H<sub>28</sub>N<sub>5</sub>O<sup>+</sup> ([M+H]<sup>+</sup>): 438.2288, found: 438.2293. HPLC column: phenomenex lux 5u cellulose -1; solvent: 2-propanol: hexane (1:5); UV light: 291 nm; flow: 1 mL /min; major enantiomer *t*<sub>r</sub> = 11.23 min, minor enantiomer *t*<sub>r</sub> = 20.29 min.

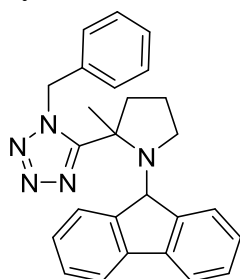
### 5-((2*R*,5*R*)-1-(9*H*-fluoren-9-yl)-5-methylpyrrolidin-2-yl)-1-benzyl-1*H*-tetrazole (*rac*-19h) 5-



**(1-(9*H*-fluoren-9-yl)-2-methylpyrrolidin-2-yl)-1-benzyl-1*H*-tetrazole (19h')**: According to the general procedure II: 9-fluorenone imine (0.3 mmol, 1.2 equiv, 54 mg), *rac* 2-methyl pyrrolidine (0.75 mmol, 3 equiv, 78  $\mu$ L), trimethylsilyl azide (0.25 mmol, 1 equiv, 33  $\mu$ L) and benzyl isocyanide (0.25 mmol, 1 equiv, 30 mg) and acetic acid (0.25 mmol, 1 equiv, 15  $\mu$ L) in neat condition were reacted for 12 hours. The crude product was purified by SiO<sub>2</sub> column chromatography (ethyl acetate: hexane; 1:1) to obtain **rac-19h** as brown compound (49 mg, 48%) and **19h'** (24 mg, 24%) as brown compound. The regioisomeric ratio of **rac-19h** and **19h'** is (2.1:1).

Analytical data for (**rac-19h**): FTIR (KBr):  $\tilde{\nu}$  = 3046, 2963, 1607, 1452, 1383, 1128, 1075, 745, 722  $\text{cm}^{-1}$ .  $^1\text{H}$  NMR (600 MHz,  $\text{CDCl}_3$ )  $\delta$  = 7.81 (d,  $J$  = 7.2 Hz, 1H), 7.66 – 7.62 (m, 2H), 7.50 – 7.47 (m, 1H), 7.35 – 7.33 (m, 1H), 7.29 – 7.28 (m, 1H), 7.22 – 7.15 (m, 4H), 7.08 – 7.05 (m, 1H), 6.69 (d,  $J$  = 7.2 Hz, 2H), 5.28 (d,  $J$  = 15.6 Hz, 1H), 5.10 (s, 1H), 4.26 (d,  $J$  = 15.6 Hz, 1H), 3.85 – 3.83 (m, 1H), 3.76 – 3.71 (m, 1H), 2.02 – 1.97 (m, 1H), 1.92 – 1.88 (m, 1H), 1.66 – 1.64 (m, 1H), 1.54 – 1.49 (m, 1H), 1.41 (d,  $J$  = 6.0 Hz, 3H).  $^{13}\text{C}$  NMR (151 MHz,  $\text{CDCl}_3$ )  $\delta$  = 158.5, 144.2, 144.1, 141.7, 139.7, 134.3, 129.1, 128.9, 128.6, 128.5, 127.6, 127.4, 127.1, 126.2, 126.0, 120.4, 119.7, 63.6, 59.1, 52.3, 50.0, 33.0, 30.9, 20.9 ppm. HRMS (ESI) exact mass calculated for  $\text{C}_{26}\text{H}_{26}\text{N}_5^+([\text{M}+\text{H}]^+)$ : 408.2183, found: 408.2188.

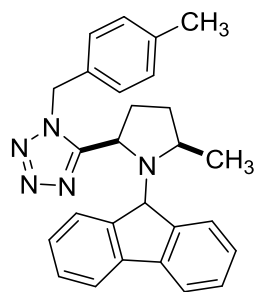
Analytical data for (**19h'**): FTIR (KBr):  $\tilde{\nu}$  = 3063, 2926, 1649, 1452, 1108, 1068, 744, 736, 702



$\text{cm}^{-1}$ .  $^1\text{H}$  NMR (600 MHz,  $\text{CDCl}_3$ )  $\delta$  = 7.78 (d,  $J$  = 7.2 Hz, 1H), 7.64 (d,  $J$  = 7.2 Hz, 1H), 7.59 (d,  $J$  = 7.2 Hz, 1H), 7.53 – 7.50 (m, 1H), 7.47 – 7.45 (m, 1H), 7.32 (d,  $J$  = 7.5 Hz, 1H), 7.24 – 7.22 (m, 1H), 7.19 – 7.15 (m, 3H), 7.10 – 7.07 (m, 1H), 6.57 (d,  $J$  = 6.6 Hz, 2H), 5.18 (s, 1H), 4.98 (d,  $J$  = 15.0 Hz, 1H), 4.31 – 4.10 (m, 1H), 3.73 (s, 1H), 2.59 – 2.53 (m, 1H), 1.97 – 1.91 (m, 1H), 1.59 – 1.56 (m, 1H), 1.54 – 1.50 (m, 1H), 1.41 (s, 3H).  $^{13}\text{C}$  NMR (151 MHz,  $\text{CDCl}_3$ )  $\delta$  = 157.1, 144.4, 144.3, 140.8, 139.0, 134.4, 129.0, 128.9, 128.6, 128.1, 127.7, 127.6, 127.0, 126.6, 125.8, 120.2, 119.7, 60.9, 54.5, 50.0, 49.9, 32.0, 29.5, 19.8. HRMS (ESI) exact mass calculated for  $\text{C}_{26}\text{H}_{26}\text{N}_5^+([\text{M}+\text{H}]^+)$ : 408.2183, found: 408.2173.

**5-((2R,5R)-1-(9H-fluoren-9-yl)-5-methylpyrrolidin-2-yl)-1-(4-methylbenzyl)-1H-tetrazole (**rac-19i**) and 5-(1-(9H-fluoren-9-yl)-2-methylpyrrolidin-2-yl)-1-(4-methylbenzyl)-1H-tetrazole (**rac-19i'**):** According to the general procedure II : 9-fluorenone imine (0.30 mmol, 1.2 equiv, 54 mg), *rac* 2-methyl pyrrolidine (0.75 mmol, 3 equiv, 78  $\mu\text{L}$ ), trimethylsilyl azide (0.25 mmol, 1 equiv, 33  $\mu\text{L}$ ) and *para*-methyl benzyl isocyanide (0.25 mmol, 1 equiv, 34 mg) and acetic acid (0.13 mmol, 1 equiv, 15  $\mu\text{L}$ ) in neat condition were reacted for 12 hours. The crude product was purified by  $\text{SiO}_2$  column chromatography (ethyl acetate: hexane;1:1) to obtain **rac-19i** as brown solid (55 mg, 52%) and **19i'** (26 ,25%) as brown solid. The region-isomeric ratio of **rac-19i** and **19i'** is 2.1:1.

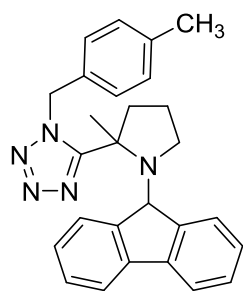
Analytical data for (**rac-19i**): FTIR (KBr):  $\tilde{\nu}$  = 2961, 2924, 1630, 1449, 1261, 1101, 1020, 800,



745  $\text{cm}^{-1}$ .  $^1\text{H}$  NMR (600 MHz,  $\text{CDCl}_3$ )  $\delta$  = 7.80 (d,  $J$  = 7.2 Hz, 1H), 7.66 – 7.63 (m, 2H), 7.50 – 7.47 (m, 1H), 7.35 – 7.33 (m, 1H), 7.29 – 7.27 (m, 1H), 7.21 (d,  $J$  = 7.2 Hz, 1H), 7.07– 7.05 (m, 1H), 6.97 – 6.96 (m, 2H), 6.59 – 6.57 (m, 2H), 5.23 (d,  $J$  = 15.6 Hz, 1H), 5.10 (s, 1H), 4.24 (d,  $J$  = 15.6 Hz, 1H), 3.88 – 3.85 (m, 1H), 3.75 – 3.70 (m, 1H), 2.25 (s, 3H), 2.02 – 1.97 (m, 1H), 1.94 – 1.89 (m, 1H), 1.71 – 1.66 (m, 1H), 1.56 – 1.51 (m, 1H), 1.40 (d,

$J$  = 6.0 Hz, 3H).  $^{13}\text{C}$  NMR (151 MHz,  $\text{CDCl}_3$ )  $\delta$  = 158.4, 144.2, 144.1, 141.7, 139.7, 138.4, 131.3, 129.7, 128.8, 128.6, 127.6, 127.4, 127.1, 126.2, 126.0, 120.4, 119.7, 63.6, 59.1, 52.3, 49.9, 33.0, 30.9, 29.9, 21.3, 20.9. ppm.  $^{13}\text{C}$  NMR (151 MHz,  $\text{CDCl}_3$ )  $\delta$  = 157.1, 144.4, 144.3, 140.8, 139.0, 138.4, 131.4, 129.7, 128.8, 128.1, 127.7, 127.6, 127.0, 126.6, 125.8, 120.2, 119.7, 60.9, 54.5, 50.0, 49.8, 32.1, 29.5, 21.2, 19.9 ppm. HRMS (ESI) exact mass calculated for  $\text{C}_{27}\text{H}_{28}\text{N}_5^+([\text{M}+\text{H}]^+)$ : 422.2339, found: 422.2329.

Analytical data for (**19i'**): FTIR (KBr):  $\tilde{\nu}$  = 2957, 2924, 2855, 1630, 1450, 1261, 1076, 742, 732



$\text{cm}^{-1}$ .  $^1\text{H}$  NMR (600 MHz, Chloroform-*d*)  $\delta$  7.77 (d,  $J$  = 7.2 Hz, 1H), 7.63 (d,  $J$  = 7.2 Hz, 1H), 7.59 (d,  $J$  = 7.8 Hz, 1H), 7.52–7.49 (m, 1H), 7.46 – 7.44 (m, 1H), 7.31 (d,  $J$  = 7.2 Hz, 1H), 7.24 – 7.21 (m, 1H), 7.09 – 7.07 (m, 1H), 6.95 (d,  $J$  = 7.8 Hz, 2H), 6.47 – 6.44 (m, 2H), 5.16 (s, 1H), 4.94 (d,  $J$  = 15.0 Hz, 1H), 4.31 – 4.24 (m, 1H), 4.15 – 4.08 (m, 1H), 3.76 – 3.63 (s, 1H), 2.59 – 2.53 (m, 1H), 2.23 (s, 3H), 1.98 – 1.92 (m, 1H), 1.55 – 1.50 (m, 1H), 1.40 (s,

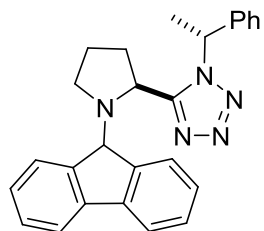
3H).  $^{13}\text{C}$  NMR (151 MHz,  $\text{CDCl}_3$ )  $\delta$  = 158.5, 144.2, 144.1, 141.7, 139.7, 134.3, 129.1, 128.9, 128.6, 128.5, 127.6, 127.4, 127.1, 126.2, 126.0, 120.4, 119.7, 63.6, 59.1, 52.3, 50.0, 33.0, 30.9, 20.9 ppm. HRMS (ESI) exact mass calculated for  $\text{C}_{27}\text{H}_{28}\text{N}_5^+([\text{M}+\text{H}]^+)$ : 422.2339, found: 422.2396.

### 5-((S)-1-(9H-fluoren-9-yl)pyrrolidin-2-yl)-1-((R)-1-phenylethyl)-1H-tetrazole (**23**) and 5-((R)-1-(9H-fluoren-9-yl)pyrrolidin-2-yl)-1-((R)-1-phenylethyl)-1H-tetrazole (**d-23**):

According to the general procedure I: 9-fluorenone imine (0.15 mmol, 1.2 equiv, 27 mg), pyrrolidine (0.75 mmol, 3 equiv, 62  $\mu\text{L}$ ), trimethylsilyl azide (0.25 mmol, 1 equiv, 34  $\mu\text{L}$ ) and (*R*)-(1-isocyanoethyl)benzene (0.25 mmol, 1 equiv, 33mg) in 4 mL methanol were reacted for 14 hours. The crude product was purified by  $\text{SiO}_2$  column chromatography (ethyl acetate: hexane;

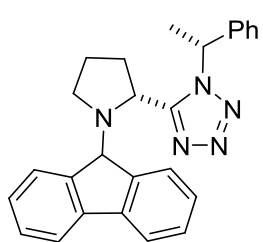
1:6) to obtain 5-((R)-1-(9H-fluoren-9-yl)pyrrolidin-2-yl)-1-((S)-1-phenylethyl)-1H-tetrazole (**23**) as brown solid (35 mg, 34% ) and 5-((S)-1-(9H-fluoren-9-yl)pyrrolidin-2-yl)-1-((R)-1-phenylethyl)-1H-tetrazole (36 mg, 35%) (**d-23**).

Analytical data for (**23**): FTIR (KBr):  $\tilde{\nu}$  = 3065, 2810, 1493, 1448, 1301, 1140, 742, 624  $\text{cm}^{-1}$



$^1\text{H NMR}$  (400 MHz,  $\text{CDCl}_3$ )  $\delta$  = 7.79 (d,  $J$  = 7.2 Hz, 1H), 7.67 (d,  $J$  = 7.6 Hz, 1H), 7.50 – 7.43 (m, 2H), 7.32 – 7.27 (m, 3H), 7.18 – 7.17 (m, 3H), 7.10 – 7.06 (m, 1H), 6.68 – 6.67 (m, 2H), 5.05 (s, 1H), 4.60 – 4.55 (m, 1H), 3.85 – 3.82 (m, 1H), 3.51 – 3.46 (m, 1H), 3.24 – 3.17 (m, 1H), 2.25 – 2.13 (m, 1H), 1.87 – 1.77 (m, 1H), 1.65 (d,  $J$  = 6.4 Hz, 3H), 1.62 – 1.57 (m, 2H)  $^{13}\text{C NMR}$  (151 MHz,  $\text{CDCl}_3$ )  $\delta$  = 158.0, 144.0, 143.5, 141.3, 140.6, 140.0, 128.8, 128.5, 128.3, 127.6, 126.7, 126.2, 125.7, 120.0, 119.5, 65.4, 57.9, 52.2, 51.5, 32.6, 24.3, 22.4 ppm. HRMS (ESI) exact mass calculated for  $\text{C}_{26}\text{H}_{26}\text{N}_5^+$  ( $[\text{M}+\text{H}]^+$ ): 408.2183, found: 408.2171. The enantiomeric excess (>96 %) was determined by HPLC analysis: column: phenomenex lux 5u cellulose -1; solvent: 2-propanol: hexane (1:9); UV light: 291 nm; flow: 1 mL /min; major enantiomer  $t_r$  = 14.62 min, minor enantiomer  $t_r$  = 11.28 min.

Analytical data for (**d-23**): FTIR (KBr):  $\tilde{\nu}$  = 3065, 2810, 1493, 1448, 1301, 1140, 742, 624  $\text{cm}^{-1}$

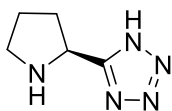


$^1\text{H NMR}$  (400 MHz,  $\text{CDCl}_3$ )  $\delta$  = 7.69 – 7.67 (m, 2H), 7.62 (d,  $J$  = 7.6 Hz, 1H), 7.56 (d,  $J$  = 7.6 Hz, 1H), 7.42 – 7.33 (m, 8H), 7.24 – 7.20 (m, 1H), 6.69 (q,  $J$  = 7.1 Hz, 1H), 4.97 – 4.93 (m, 1H), 4.69 (s, 1H), 2.73 – 2.68 (m, 1H), 2.22 – 2.17 (m, 1H), 2.13 (d,  $J$  = 7.1 Hz, 3H), 2.06 – 1.99 (m, 1H), 1.75 – 1.76 (m, 1H), 1.66 – 1.60 (m, 1H), 1.55 – 1.49 (m, 1H).  $^{13}\text{C NMR}$  (151 MHz,  $\text{CDCl}_3$ )  $\delta$  = 155.1, 144.3, 141.8, 141.6, 140.8, 140.4, 129.3, 128.7, 128.7, 128.6, 127.7, 127.3, 126.8, 126.3, 124.9, 120.2, 120.1, 63.7, 58.6, 56.1, 46.7, 30.5, 24.0, 22.7 ppm. HRMS (ESI) exact mass calculated for  $\text{C}_{26}\text{H}_{26}\text{N}_5^+$  ( $[\text{M}+\text{H}]^+$ ): 408.2183, found: 408.2191. The enantiomeric excess (>96 %) was determined by HPLC analysis; column: phenomenex lux 5u cellulose -1; solvent: 2-propanol: hexane (1:5); light: 291 nm; flow: 1 mL /min; major enantiomer  $t_r$  = 14.88 min, minor enantiomer  $t_r$  = 7.05 min.



**Reaction of *L* proline with 9-fluorenone imine :** According to the general procedure I: 9-fluorenone imine (0.3 mmol, 1.2 equiv, 54 mg), *L*-proline (0.75 mmol, 3 equiv, 87 mg), trimethylsilyl azide (0.25 mmol, 1 equiv, 34  $\mu$ L ) and (*R*)-(1-isocyanoethyl)benzene (0.25 mmol, 1 equiv, 33mg) in 4 mL methanol were reacted for 14 hours. The crude product was purified by SiO<sub>2</sub> column chromatography (ethyl acetate: hexane; 1:6) to obtain 5-((*R*)-1-(9H-fluoren-9-yl)pyrrolidin-2-yl)-1-((*S*)-1-phenylethyl)-1H-tetrazole (**23**) as brown solid (44 mg, 44 %) and 5-((*S*)-1-(9H-fluoren-9-yl)pyrrolidin-2-yl)-1-((*R*)-1-phenylethyl)-1H-tetrazole (42 mg, 42 %) (**d-23**).

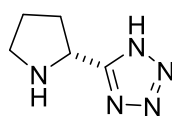
**(S)-5-(pyrrolidin-2-yl)-1H-tetrazole (21):** 5-((*S*)-1-(9H-fluoren-9-yl)pyrrolidin-2-yl)-1-((*R*)-1-



phenylethyl)-1H-tetrazole (**23**) ( 0.28 mmol, 1 equiv, 115 mg) was dissolved in ethyl acetate and methanol (3:1, v/v). Palladium (10%) on charcoal (0.49 mmol, 2 equiv, 56 mg) was added to it. Then the flask was evacuated and re-filled with

hydrogen. The process was repeated three times. Then, the reaction mixture was kept on shaking at 40 PSI of hydrogen for 72 hours. After the completion of the reaction, the reaction mixture was filtered through a pad of celite, and the celite pad was washed successively with methanol (5 $\times$ 5 mL) and of ethyl acetate (2 $\times$ 5 mL). The filtrate was concentrated under reduce pressure to obtain brown gummy compound which was washed with distilled hexane (3 $\times$ 10 mL) and chloroform (10 $\times$ 3 mL) successively. Finally, the residual solvent was removed under reduced pressure to obtain the analytically pure compound **21** as brown solid (28 mg, 72%). FTIR (KBr):  $\tilde{\nu}$  = .  $[\alpha]_D^{25}$  = -8.75 (MeOH, c = 0.80) (reported value:  $[\alpha]_D^{26}$  = - 8.57 (MeOH, c = 0.63)).<sup>1</sup> <sup>1</sup>H NMR (600 MHz, MeOD)  $\delta$  = 3.48 – 3.43 (m, 2H), 2.55 – 2.50 (m, 1H), 2.37 – 2.33 (m, 1H), 2.29 – 2.26 (m, 1H), 2.22 – 2.16 (m, 1H). HRMS (ESI) exact mass calculated for C<sub>5</sub>H<sub>10</sub>N<sub>5</sub><sup>+</sup> ([M+H]<sup>+</sup>): 140.0931, found: 140.0933.

**(R)-5-(pyrrolidin-2-yl)-1H-tetrazole (ent-21):** 5-((*R*)-1-(9H-fluoren-9-yl)pyrrolidin-2-yl)-1-



((*R*)-1-phenylethyl)-1H-tetrazole (**d-23**) ( 0.25 mmol, 1 equiv, 100 mg) was dissolved in ethyl acetate and methanol (3:1, v/v). Palladium (10%) on charcoal (0.5 mmol, 2 equiv, 53 mg) was added to it. Then the flask was evacuated and re-

filled with hydrogen. The process was repeated three times. Then, the reaction mixture was kept

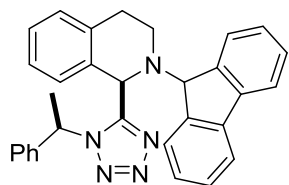
<sup>1</sup> N. Momiyama, H. Torii, S. Satio, H. Yamamoto, *Proc. Nat. Acad. Sci. U. S. A.* **2004**, *101*, 5374.

on shaking at 40 PSI of hydrogen for 72 hours. After the completion of the reaction, the reaction mixture was filtered through a pad of celite, and the celite pad was washed successively with methanol (5×5 mL) and of ethyl acetate (2× 5 mL). The filtrate was concentrated under reduce pressure to obtain a brown gummy compound which was washed with distilled hexane (3×10 mL) and chloroform (10×3 mL) successively. Finally, the residual solvent was removed under reduced pressure to obtain the analytically pure compound **ent-21** as grey solid (27 mg, 78%). FTIR (KBr):  $\tilde{\nu} = 2960, 1651, 1634, 1428, 1409, 1009, 831 \text{ cm}^{-1}$   $[\alpha]_D^{25} = +8.0$  (c= 0.80 MeOH).  $^1\text{H NMR}$  (400 MHz, DMSO)  $\delta = 4.81 - 4.77$  (m, 1H), 3.32 – 3.26 (m, 2H), 2.40 – 2.32 (m, 1H), 2.21 – 2.13 (m, 1H), 2.10 – 1.98 (m, 2H) ppm.  $^{13}\text{C NMR}$  (151 MHz, DMSO)  $\delta = 157.9, 55.1, 44.7, 30.0, 23.3$ . HRMS (ESI) exact mass calculated for  $\text{C}_5\text{H}_{10}\text{N}_5^+$  ( $[\text{M}+\text{H}]^+$ ): 140.0931, found: 140.0935.

**(R)-2-(9H-fluoren-9-yl)-1-(1-((R)-1-phenylethyl)-1H-tetrazol-5-yl)-1,2,3,4-tetrahydroisoquinoline: (24) and (S)-2-(9H-fluoren-9-yl)-1-(1-((R)-1-phenylethyl)-1H-tetrazol-5-yl)-1,2,3,4-tetrahydroisoquinoline: (d-24).**

According to the general procedure II : 9-fluorenone imine (0.15 mmol, 1.2 equiv, 27 mg), 1,2,3,4-tetrahydroisoquinoline (0.75 mmol, 3 equiv, 96  $\mu\text{L}$ ), trimethylsilyl azide (0.25 mmol, 1 equiv, 34  $\mu\text{L}$ ) and (*R*)-(1-isocyanoethyl)benzene (0.25 mmol, 1 equiv, 33mg) in 4 mL methanol were reacted for 24 hours. After the completion of the reaction, the solid product was precipitated from the reaction mixture. Then the solid product was washed with (3×5 mL) methanol to obtain (**24**) as white solid (40 mg). Next, mother liquor was evaporated under reduced pressure. The crude product was purified by  $\text{SiO}_2$  column chromatography (ethyl acetate: hexane; 1:20) to obtain additional amount (**24**) (10 mg) and (**24**) (26 mg, 22%). The combined yield of (**24**) is (50 mg, 43%).

Analytical data for (**24**): FTIR (KBr):  $\tilde{\nu} = 3035, 3020, 2923, 1650, 1450, 1433, 1377, 1240, 736,$

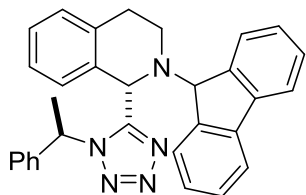


$722 \text{ cm}^{-1}$ .  $[\alpha]_D^{25} = + 210.77$  (c= 0.26,  $\text{CHCl}_3$ ).  $^1\text{H NMR}$  (400 MHz,  $\text{CDCl}_3$ )  $\delta = 8.03$  (d,  $J = 7.2 \text{ Hz}$ , 1H), 7.71 (t,  $J = 7.6 \text{ Hz}$ , 2H), 7.52 (d,  $J = 7.2 \text{ Hz}$ , 1H), 7.41 (q,  $J = 7.73 \text{ Hz}$ , 2H), 7.36 – 7.28 (m, 2H), 7.10 – 7.03 (m, 2H), 7.02 – 6.95 (m, 3H), 6.71 (d,  $J = 7.6 \text{ Hz}$ , 2H), 6.58 (t,  $J = 7.6 \text{ Hz}$ ,

1H), 6.52 (s, 1H), 6.30 – 6.25 (m, 2H), 4.51 (s, 1H), 3.08 – 3.00 (m, 1H), 2.61 – 2.57 (m, 1H), 2.51 – 2.47 (m, 1H), 2.43 – 2.36 (m, 1H), 2.11 (d,  $J = 6.8 \text{ Hz}$ , 3H).  $^{13}\text{C NMR}$  (151 MHz,  $\text{CDCl}_3$ )  $\delta = 154.8, 143.8, 141.8, 141.5, 141.4, 138.5, 134.6, 132.6, 129.1, 128.9, 128.8, 128.5, 127.8, 127.6,$

127.5, 127.2, 126.6, 126.5, 124.5, 120.4, 120.0, 65.8, 58.9, 58.0, 42.9, 29.9, 24.0 ppm . HRMS (ESI) exact mass calculated for  $C_{31}H_{28}N_5^+$  ( $[M+H]^+$ ): 470.2339, found: 470.2345. The enantiomeric excess (>92%) was determined by HPLC column: chiralpak IA; solvent: 2-propanol: hexane (3:97); light: 291 nm; flow: 1mL /min; major enantiomer  $t_r = 12.81$  min, minor enantiomer  $t_r = 10.81$  min.

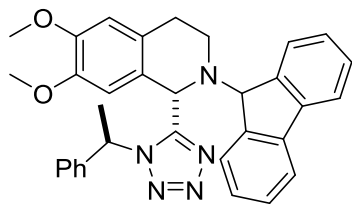
Analytical data for **(d-24)**: FTIR (KBr):  $\tilde{\nu} = 3063, 2925, 1715, 1652, 1450, 1263, 744$   $cm^{-1}$



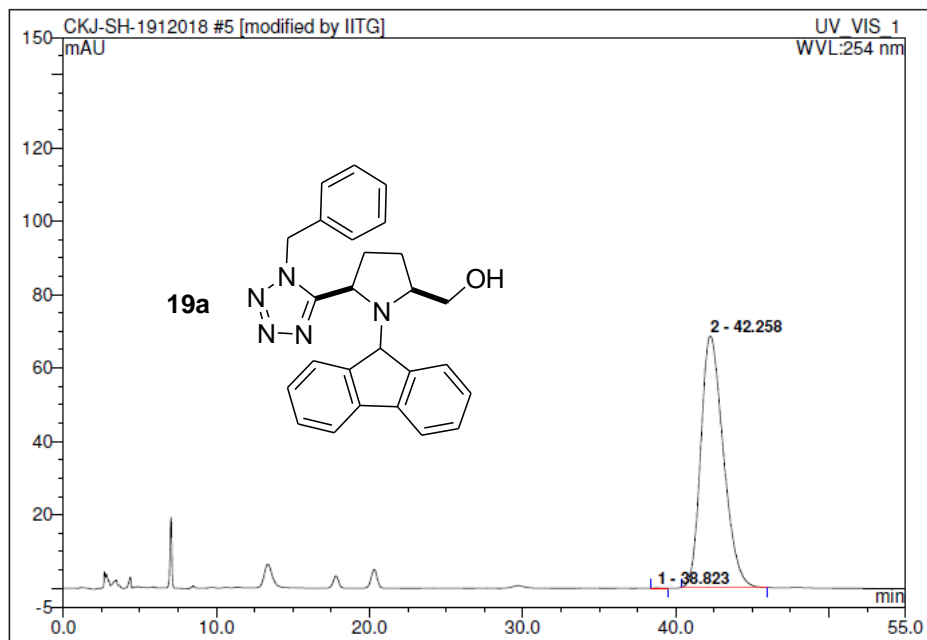
$[a]_D^{25} = -192.31$  ( $c = 0.26, CHCl_3$ ).  $^1H$  NMR (400 MHz,  $CDCl_3$ )  $\delta = 7.89$  (d,  $J = 6.4$  Hz, 1H), 7.67 (d,  $J = 7.6$  Hz, 1H), 7.61 (d,  $J = 7.6$  Hz, 1H), 7.41 – 7.29 (m, 5H), 7.27 – 7.20 (m, 6H), 7.04 (s, 1H), 6.95 – 6.91 (m, 1H), 6.35 – 6.15 (m, 3H), 5.28 (s, 1H), 4.58 (s, 1H), 3.04 – 2.96 (m,

1H), 2.73 – 2.56 (m, 3H), 1.39 (d,  $J = 7.2$  Hz, 3H).  $^{13}C$  NMR (151 MHz,  $CDCl_3$ )  $\delta = 155.9, 143.3, 142.4, 141.2, 140.9, 140.2, 135.5, 133.3, 129.6, 129.3, 128.6, 128.5, 128.4, 127.8, 127.5, 127.3, 127.0, 126.9, 126.8, 126.7, 125.4, 120.3, 119.5, 66.4, 59.0, 56.1, 43.3, 30.0, 23.1$  ppm. HRMS (ESI) exact mass calculated for  $C_{31}H_{28}N_5^+$  ( $[M+H]^+$ ): 470.2339, found: 470.2339. The enantiomeric excess (>96%) was determined by HPLC column: chiralpak IA; solvent: 2-propanol: hexane (4:96); light: 291 nm; flow: 1mL /min; major enantiomer  $t_r = 9.54$  min, minor enantiomer  $t_r = 15.7$  min.

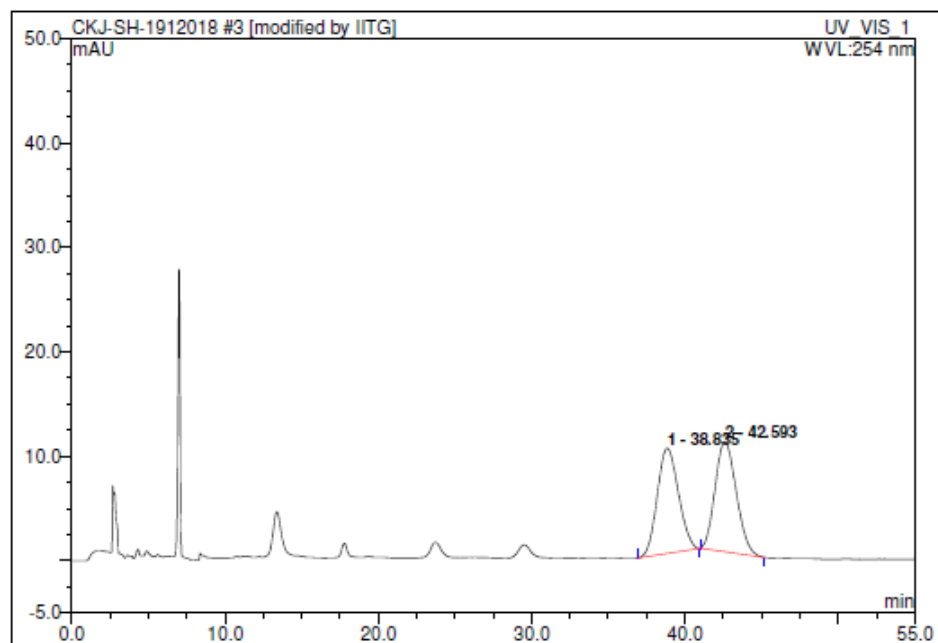
**(S)-2-(9H-fluoren-9-yl)-6,7-dimethoxy-1-(1-((R)-1-phenylethyl)-1H-tetrazol-5-yl)-1,2,3,4-tetrahydroisoquinoline (d-25)**: According to the general procedure I: 9-fluorenone imine (0.6 mmol, 1.2 equiv, 54 mg), 6,7- dimethoxy 1,2,3,4-tetrahydroisoquinoline (1.5 mmol, 3 equiv, 344), trimethylsilyl azide (0.5 mmol, 1 equiv, 68  $\mu L$ ) and (*R*)-(1-isocyanoethyl)benzene (0.5 mmol, 1 equiv, 66mg) in 6 mL methanol were reacted for 24 hours. After the completion of the reaction, the solid product was precipitated from the reaction mixture. Then the solid product was washed with (3 $\times$ 5 mL) methanol to obtain **(d-25)** as white solid (48 mg). Next, mother liquor was evaporated under reduced pressure. The crude product was purified by  $SiO_2$  column chromatography (ethyl acetate: hexane; 1:5) to obtain additional amount **(d-25)** (100 mg) compound. The combined yield of **(d-25)** is (148 mg, 56 %).



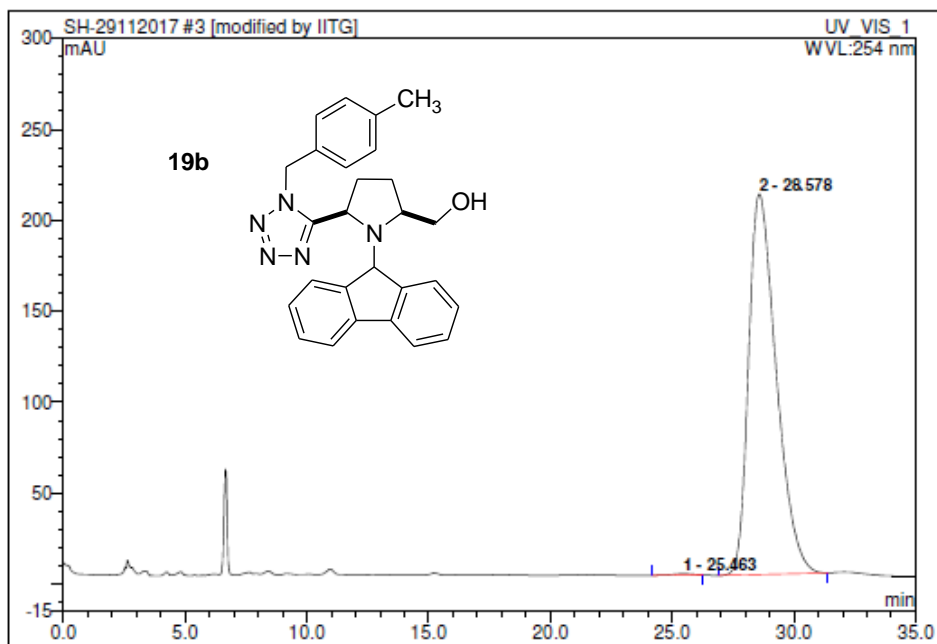
FTIR (KBr):  $\tilde{\nu}$  = 3065, 2927, 2817, 1609, 1520, 1448, 1254, 1007, 748, 768  $\text{cm}^{-1}$ .  $^1\text{H}$  NMR (600 MHz,  $\text{CDCl}_3$ )  $\delta$  = 8.01 (d,  $J$  = 7.2 Hz, 1H), 7.74 – 7.71 (m, 2H), 7.50 (d,  $J$  = 7.2 Hz, 1H), 7.44 – 7.39 (m, 2H), 7.36 – 7.34 (m, 1H), 7.31 – 7.29 (m, 1H), 7.13 – 7.11 (m, 1H), 7.03 – 7.01 (m, 2H), 6.75 (d,  $J$  = 7.2 Hz, 2H), 6.46 (s, 1H), 6.42 (s, 1H), 6.31 (q,  $J$  = 7.2 Hz, 1H), 5.55 (s, 1H), 4.51 (s, 1H), 3.80 (s, 3H), 3.16 (s, 3H), 2.98 – 2.90 (m, 1H), 2.51 – 2.40 (m, 3H), 2.12 (d,  $J$  = 7.2 Hz, 3H).  $^{13}\text{C}$  NMR (151 MHz,  $\text{CDCl}_3$ )  $\delta$  = 155.1, 148.5, 147.6, 144.0, 141.9, 141.5, 141.4, 138.9, 128.9, 128.8, 128.2, 127.9, 127.8, 127.5, 127.1, 126.7, 126.1, 124.6, 124.3, 120.5, 120.0, 111.2, 109.5, 65.9, 59.1, 57.6, 66.0, 55.4, 43.1, 29.5, 24.1. ppm.  $^{13}\text{C}$  NMR (151 MHz,  $\text{CDCl}_3$ )  $\delta$  = 155.9, 148.6, 148.0, 143.3, 142.7, 141.1, 140.9, 140.2, 129.4, 128.5, 128.5, 128.4, 127.8, 127.5, 127.4, 126.8, 125.5, 124.8, 120.3, 119.5, 111.6, 109.0, 66.8, 58.8, 60.6, 56.1, 56.0, 43.6, 29.6, 23.5 ppm. HRMS (ESI) exact mass calculated for  $\text{C}_{33}\text{H}_{32}\text{N}_5\text{O}_2^+$  ( $[\text{M}+\text{H}]^+$ ): 530.2551, found: 530.2549.



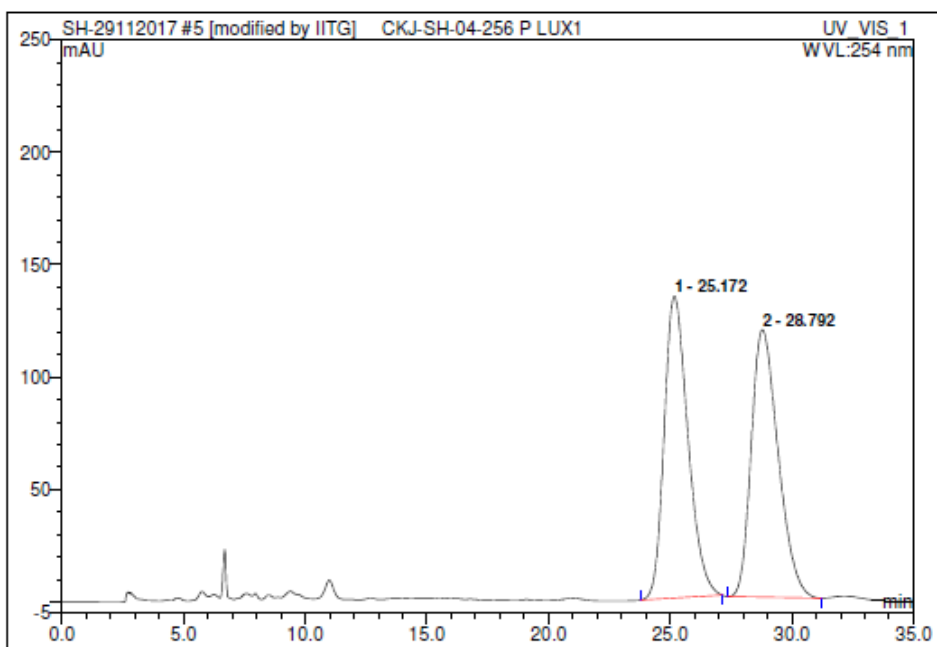
No.	Ret.Time min	Peak Name	Height mAU	Area mAU*min	Rel.Area %	Amount	Type
1	38.82	n.a.	0.027	0.015	0.01	n.a.	BMB*
2	42.26	n.a.	68.497	116.762	99.99	n.a.	BMB*
<b>Total:</b>			68.524	116.777	100.00	0.000	



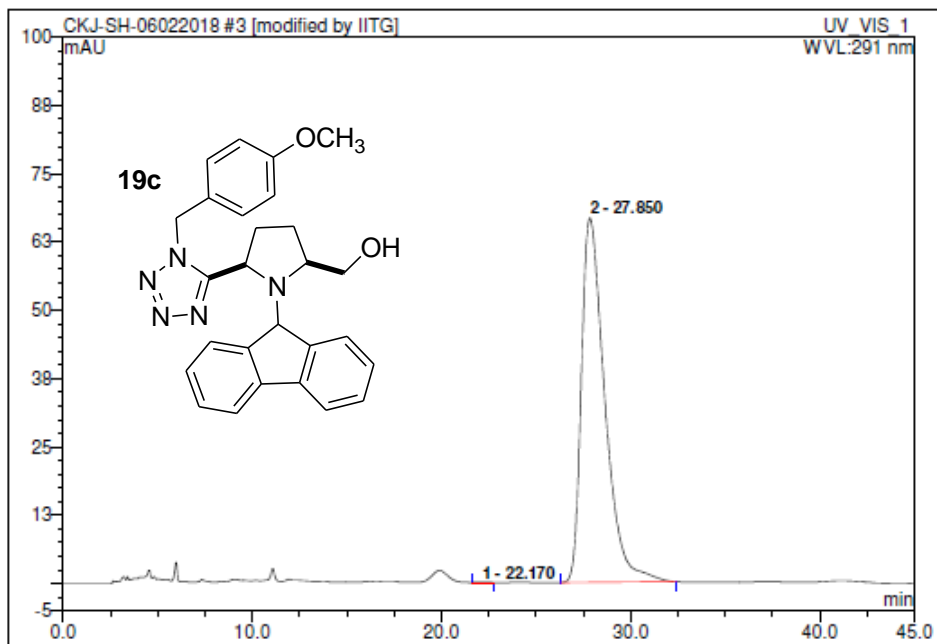
No.	Ret.Time min	Peak Name	Height mAU	Area mAU*min	Rel.Area %	Amount	Type
1	38.84	n.a.	10.093	16.155	48.92	n.a.	BMB
2	42.59	n.a.	10.548	16.869	51.08	n.a.	BMB*
<b>Total:</b>			20.642	33.025	100.00	0.000	



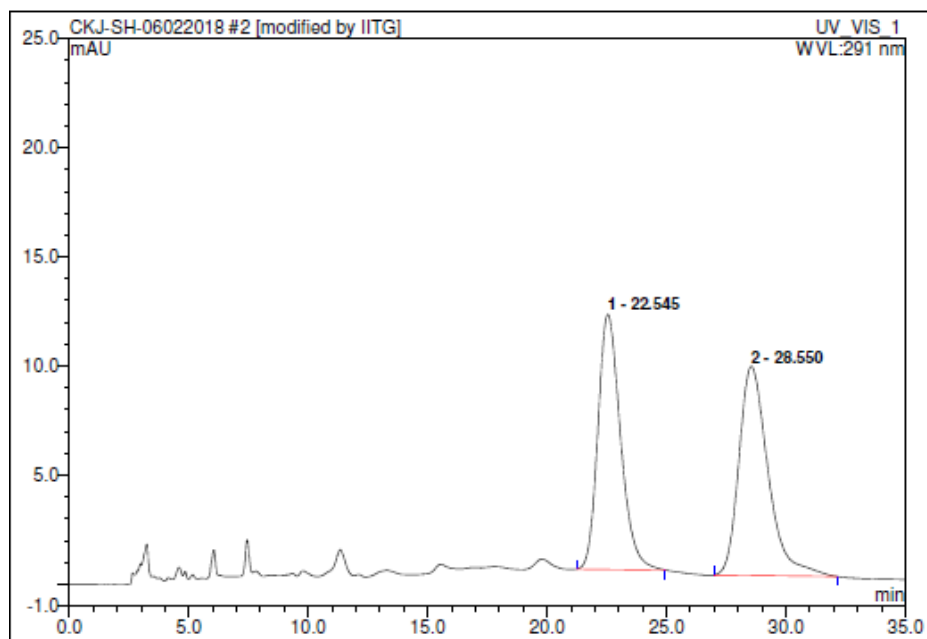
No.	Ret.Time min	Peak Name	Height mAU	Area mAU*min	Rel.Area %	Amount	Type
1	25.46	n.a.	0.834	0.802	0.29	n.a.	BMB*
2	28.58	n.a.	209.103	275.447	99.71	n.a.	BMB*
<b>Total:</b>			209.937	276.248	100.00	0.000	



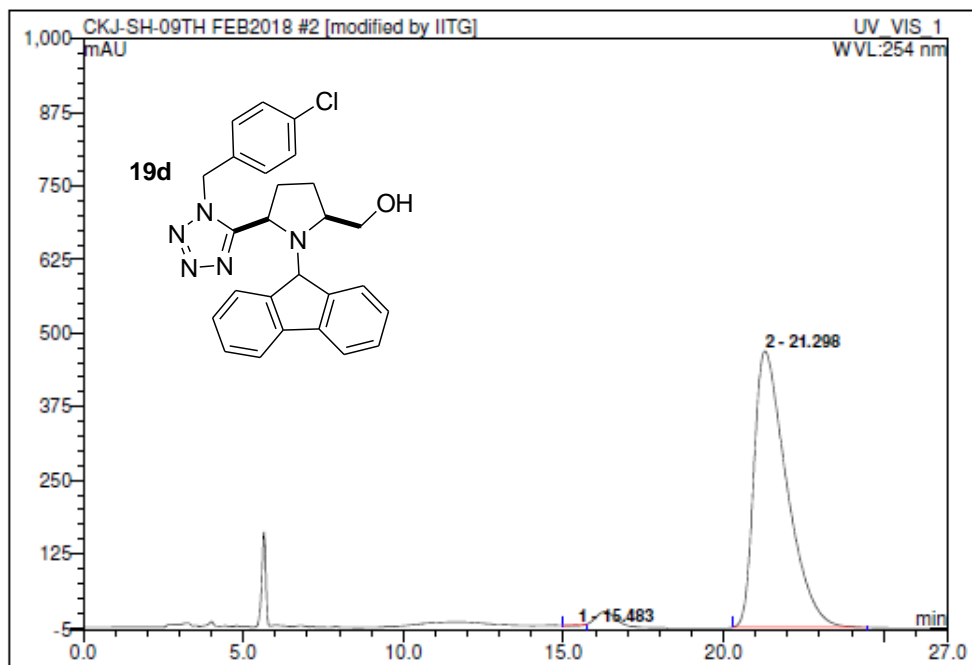
No.	Ret.Time min	Peak Name	Height mAU	Area mAU*min	Rel.Area %	Amount	Type
1	25.17	n.a.	134.287	152.041	49.97	n.a.	BMB*
2	28.79	n.a.	118.998	152.248	50.03	n.a.	BMB
<b>Total:</b>			253.284	304.289	100.00	0.000	



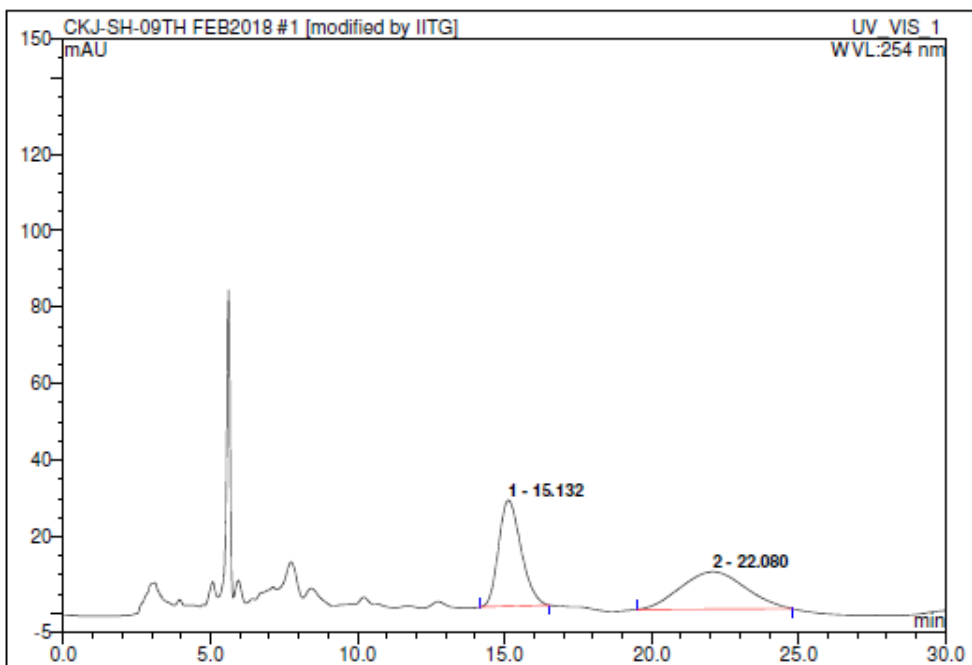
No.	Ret.Time min	Peak Name	Height mAU	Area mAU*min	Rel.Area %	Amount	Type
1	22.17	n.a.	0.030	0.019	0.02	n.a.	BMB*
2	27.85	n.a.	66.691	95.766	99.98	n.a.	BMB
<b>Total:</b>			66.720	95.785	100.00	0.000	



No.	Ret.Time min	Peak Name	Height mAU	Area mAU*min	Rel.Area %	Amount	Type
1	22.55	n.a.	11.686	12.791	48.52	n.a.	BMB*
2	28.55	n.a.	9.571	13.573	51.48	n.a.	BMB*
<b>Total:</b>			21.257	26.364	100.00	0.000	

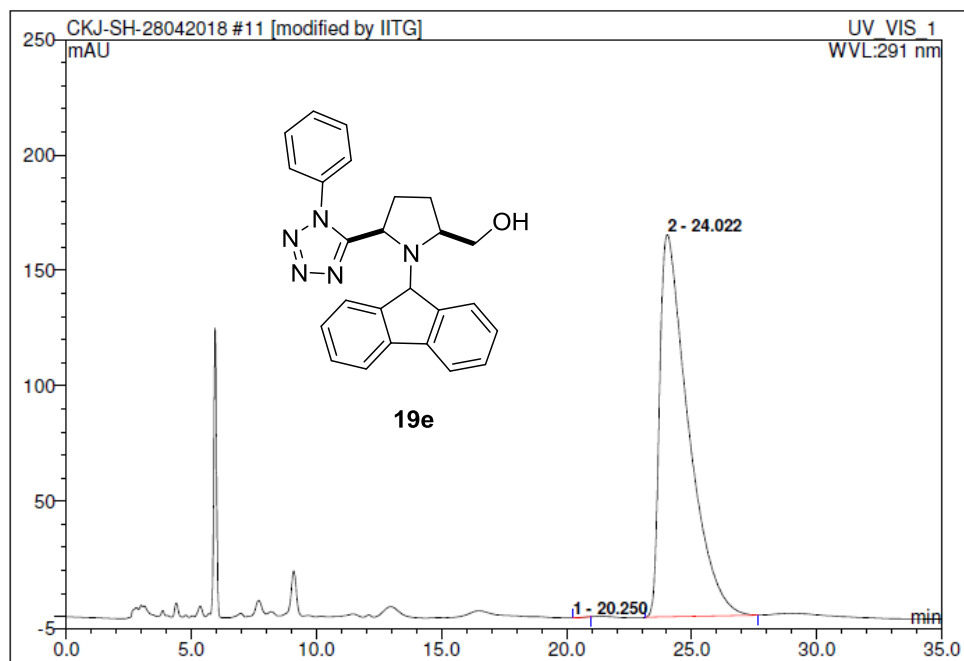


No.	Ret.Time min	Peak Name	Height mAU	Area mAU*min	Rel.Area %	Amount	Type
1	15.48	n.a.	1.691	0.808	0.15	n.a.	BMB*
2	21.30	n.a.	468.338	553.496	99.85	n.a.	BMB*
<b>Total:</b>			470.028	554.304	100.00	0.000	

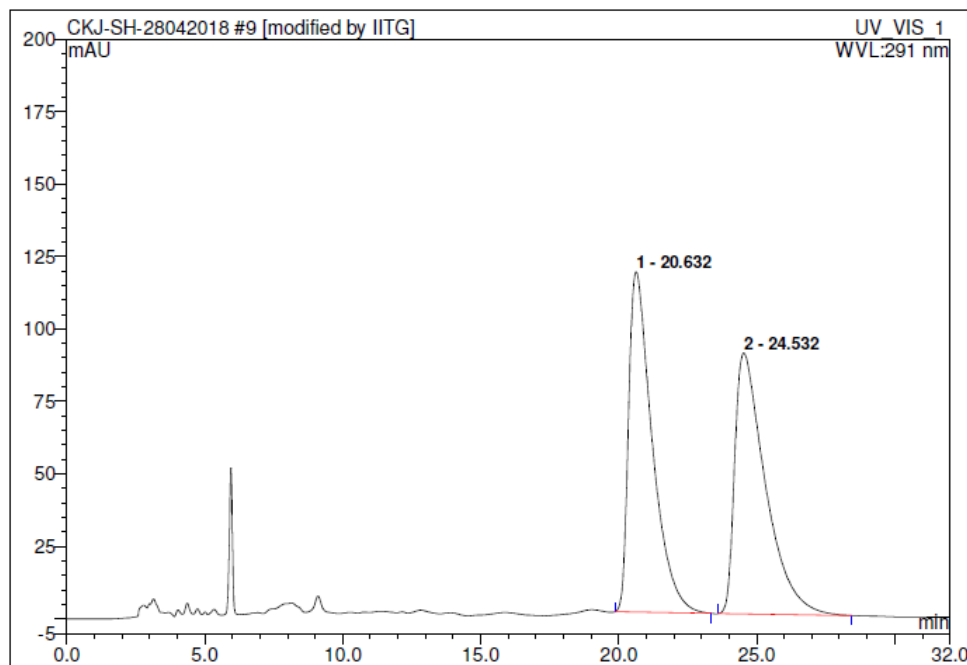


No.	Ret.Time min	Peak Name	Height mAU	Area mAU*min	Rel.Area %	Amount	Type
1	15.13	n.a.	27.694	24.616	49.81	n.a.	BMB*
2	22.08	n.a.	9.746	24.806	50.19	n.a.	BMB*
<b>Total:</b>			37.440	49.422	100.00	0.000	

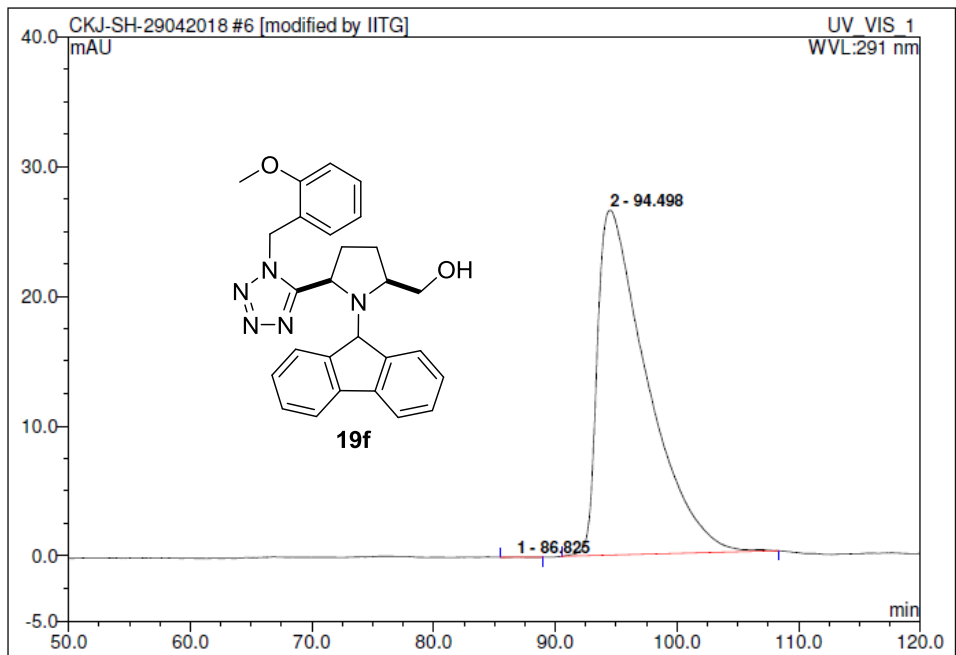




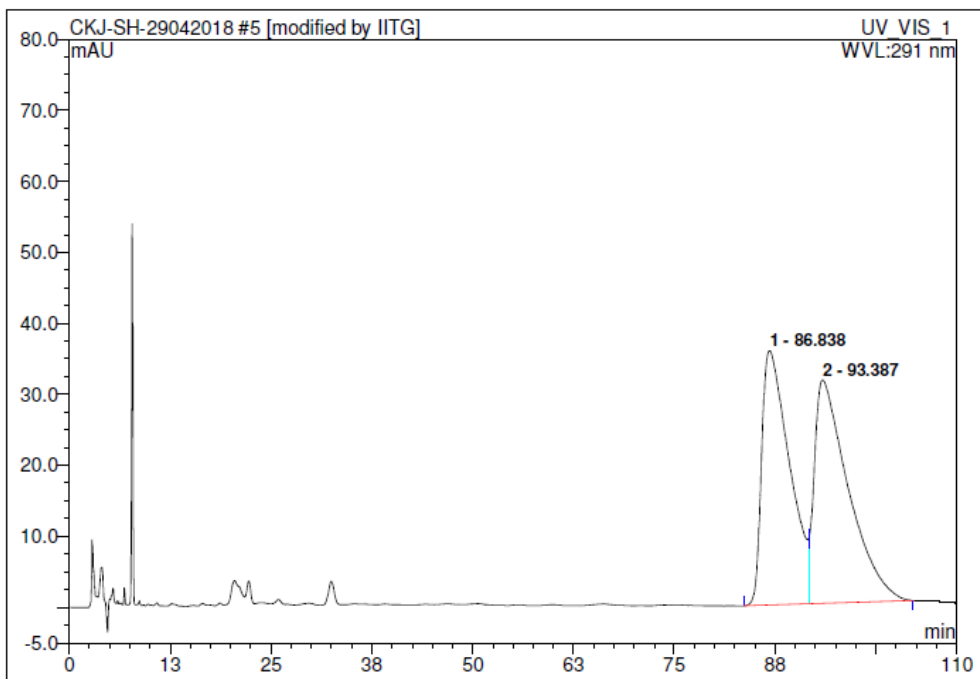
No.	Ret.Time min	Peak Name	Height mAU	Area mAU*min	Rel.Area %	Amount	Type
1	20.25	n.a.	0.008	0.036	0.02	n.a.	BMB*
2	24.02	n.a.	165.603	218.953	99.98	n.a.	BMB*
<b>Total:</b>			165.611	218.990	100.00	0.000	



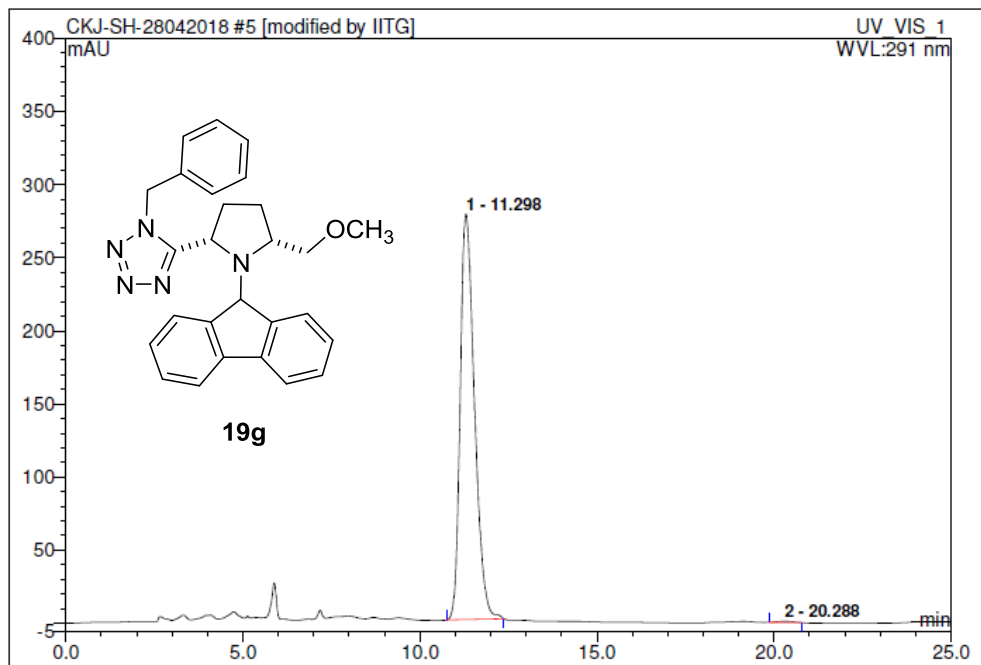
No.	Ret.Time min	Peak Name	Height mAU	Area mAU*min	Rel.Area %	Amount	Type
1	20.63	n.a.	117.378	116.269	50.08	n.a.	BMB*
2	24.53	n.a.	90.031	115.885	49.92	n.a.	BMB*
<b>Total:</b>			207.409	232.154	100.00	0.000	



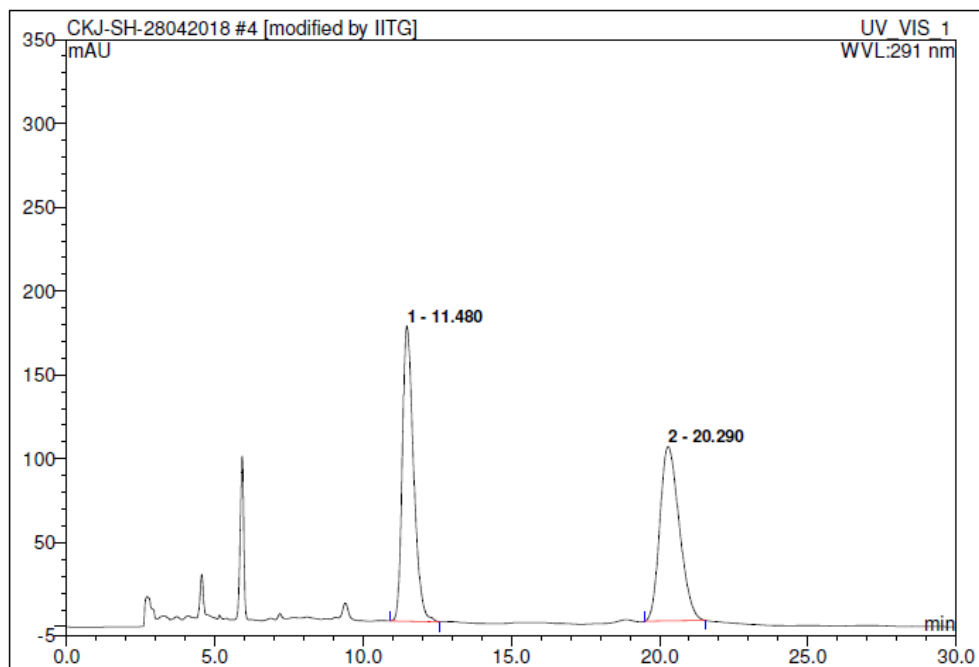
No.	Ret.Time min	Peak Name	Height mAU	Area mAU*min	Rel.Area %	Amount	Type
1	86.83	n.a.	0.016	0.015	0.01	n.a.	BMB*
2	94.50	n.a.	26.570	126.329	99.99	n.a.	BMB*
<b>Total:</b>			26.586	126.344	100.00	0.000	



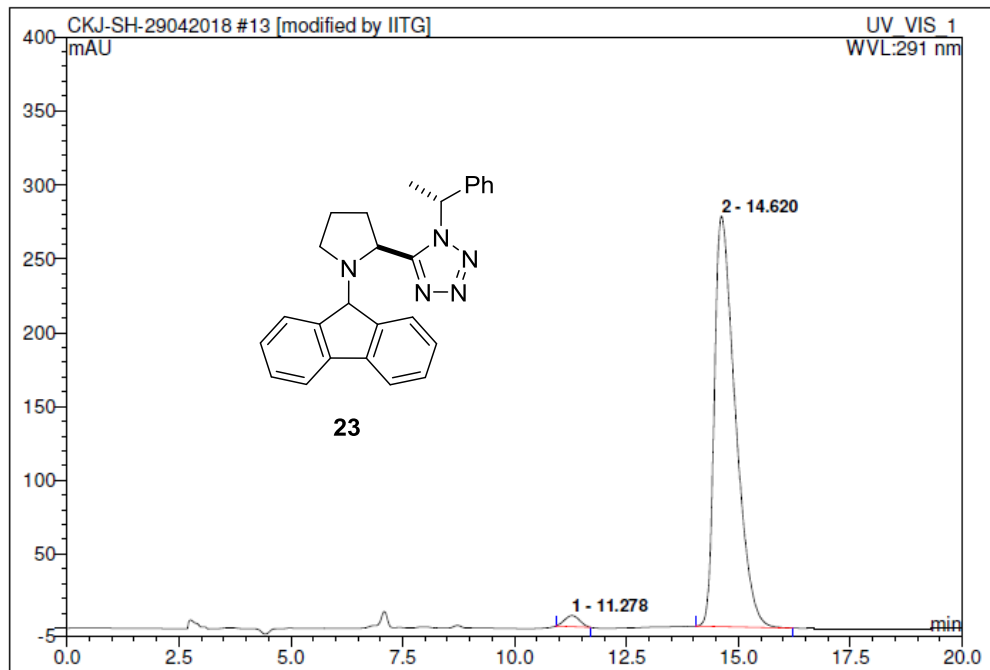
No.	Ret.Time min	Peak Name	Height mAU	Area mAU*min	Rel.Area %	Amount	Type
1	86.84	n.a.	35.827	142.398	48.00	n.a.	BM *
2	93.39	n.a.	31.429	154.277	52.00	n.a.	MB*
<b>Total:</b>			67.255	296.675	100.00	0.000	



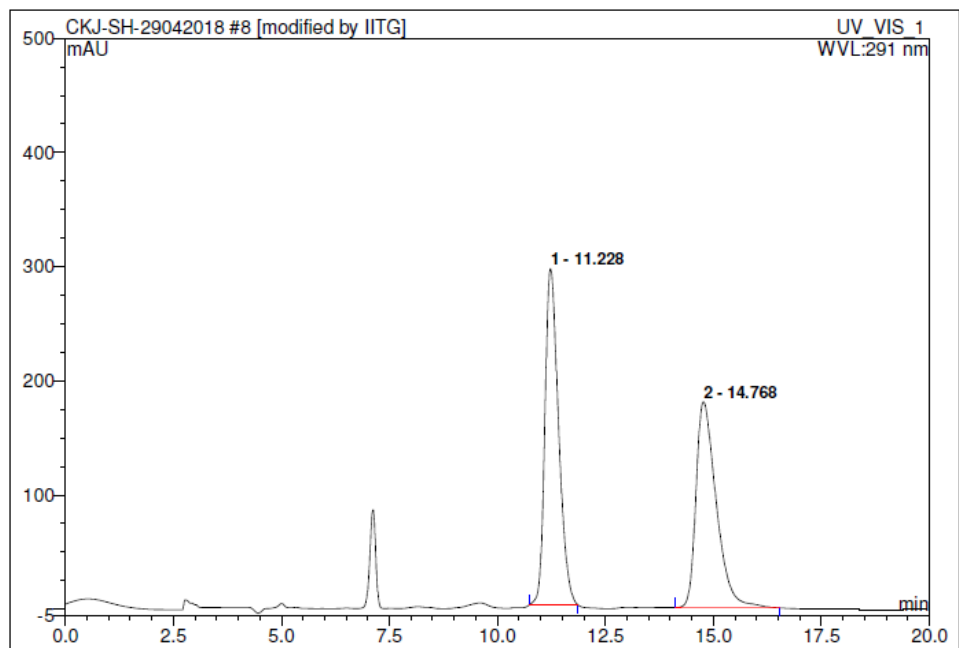
No.	Ret.Time min	Peak Name	Height mAU	Area mAU*min	Rel.Area %	Amount	Type
1	11.30	n.a.	277.213	129.207	99.69	n.a.	BMB*
2	20.29	n.a.	0.751	0.406	0.31	n.a.	BMB*
<b>Total:</b>			277.964	129.613	100.00	0.000	



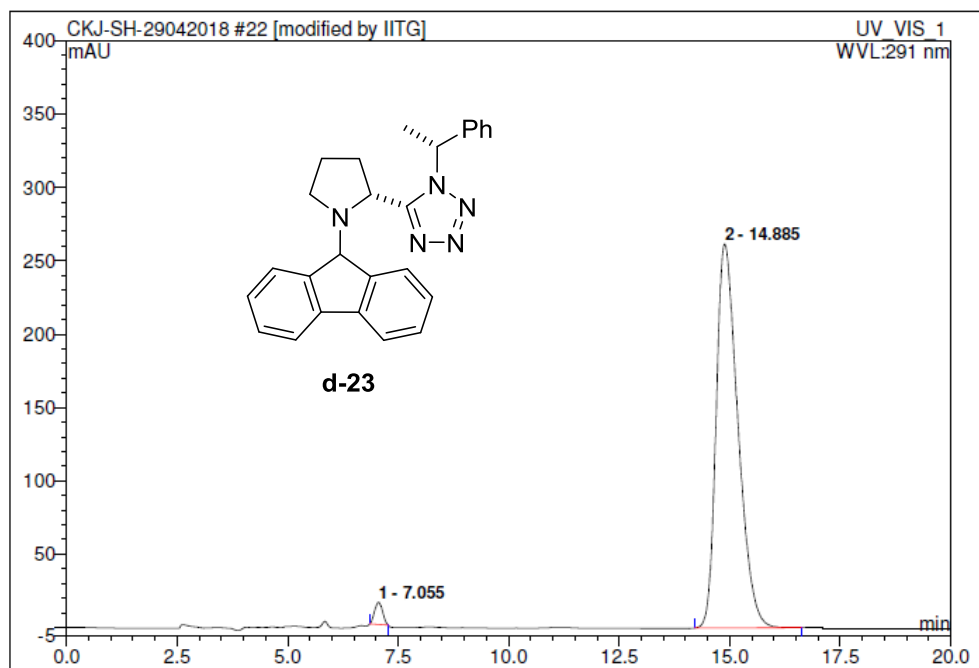
No.	Ret.Time min	Peak Name	Height mAU	Area mAU*min	Rel.Area %	Amount	Type
1	11.48	n.a.	176.127	77.607	49.53	n.a.	BMB*
2	20.29	n.a.	103.920	79.087	50.47	n.a.	BMB*
<b>Total:</b>			280.047	156.694	100.00	0.000	



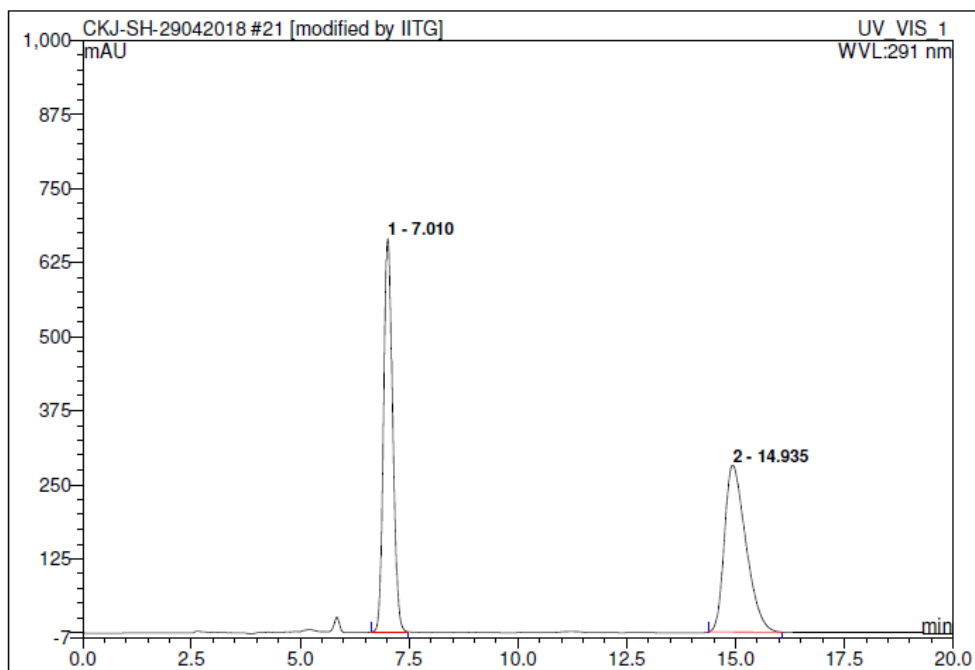
No.	Ret.Time min	Peak Name	Height mAU	Area mAU*min	Rel.Area %	Amount	Type
1	11.28	n.a.	7.534	2.925	1.91	n.a.	BMB*
2	14.62	n.a.	277.879	150.407	98.09	n.a.	BMB*
<b>Total:</b>			285.413	153.331	100.00	0.000	



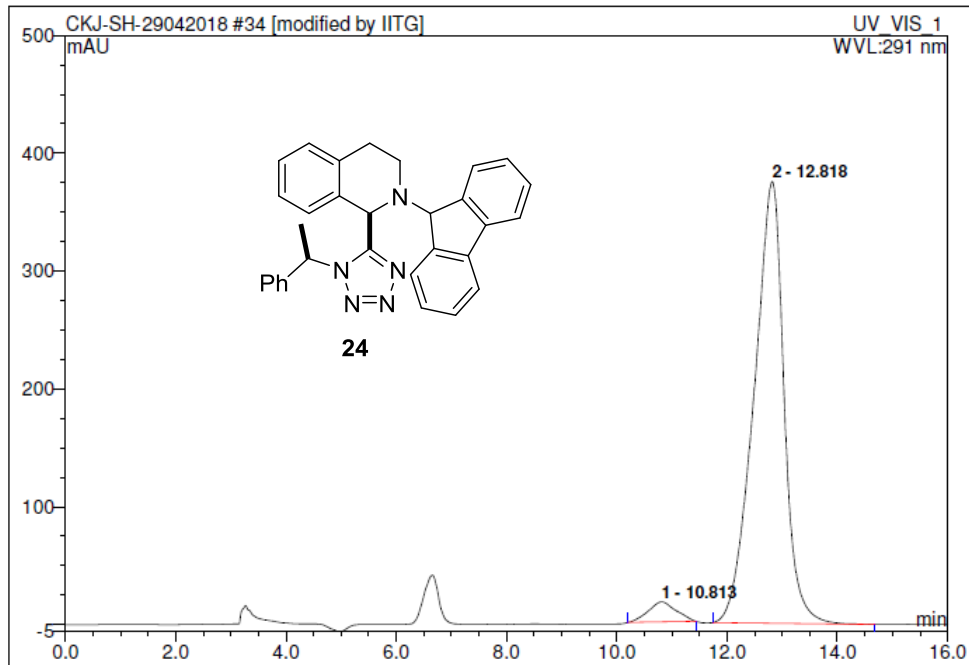
No.	Ret.Time min	Peak Name	Height mAU	Area mAU*min	Rel.Area %	Amount	Type
1	11.23	n.a.	294.102	107.333	52.23	n.a.	BMB*
2	14.77	n.a.	180.115	98.150	47.77	n.a.	BMB*
<b>Total:</b>			474.217	205.483	100.00	0.000	



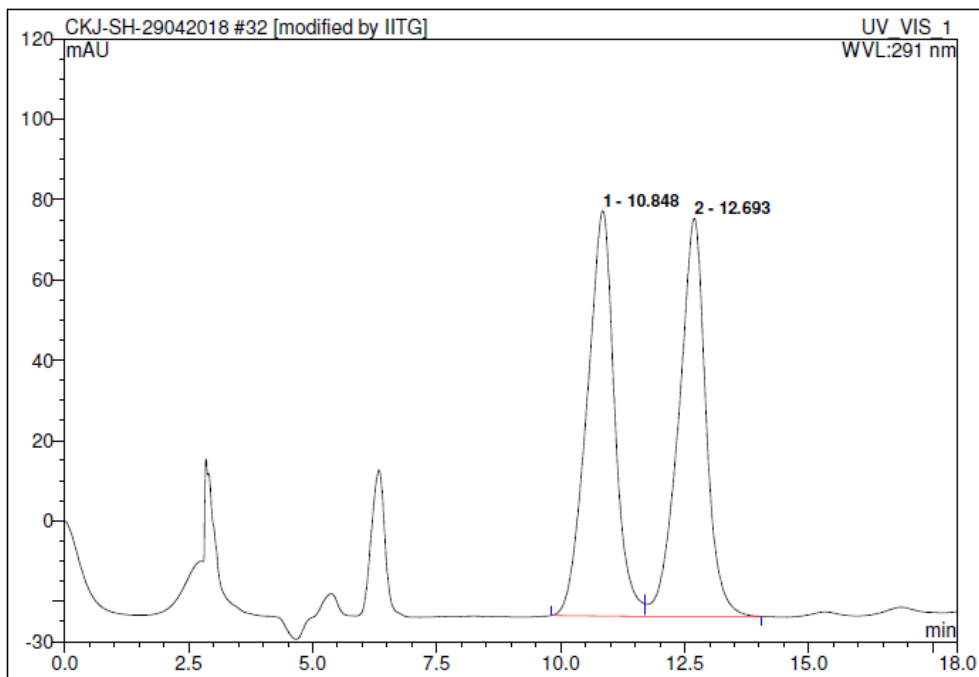
No.	Ret.Time min	Peak Name	Height mAU	Area mAU*min	Rel.Area %	Amount	Type
1	7.06	n.a.	15.079	3.157	2.07	n.a.	BMB*
2	14.89	n.a.	261.580	149.046	97.93	n.a.	BMB*
<b>Total:</b>			276.659	152.203	100.00	0.000	



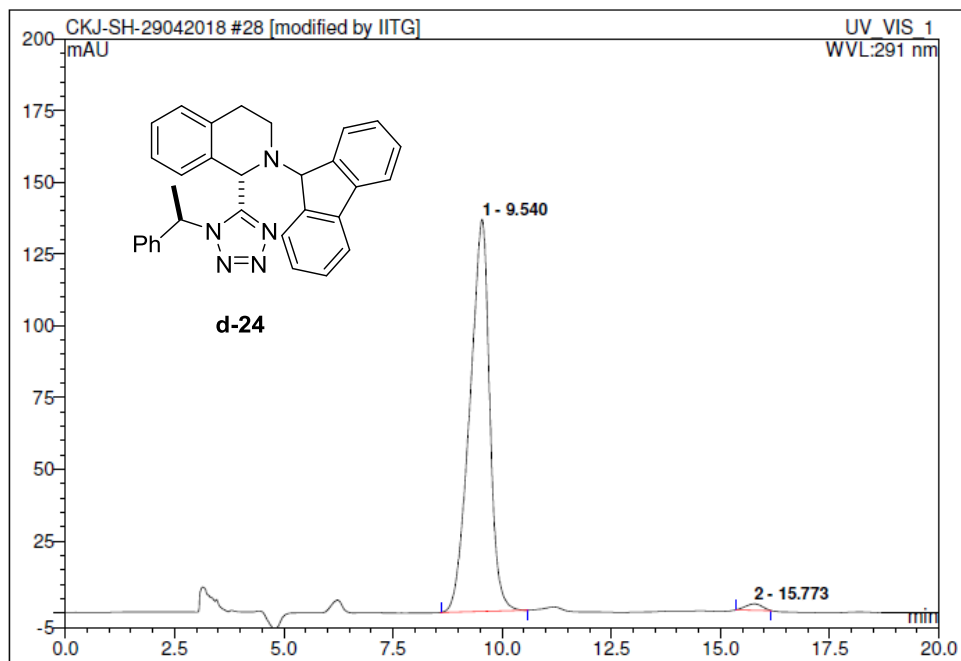
No.	Ret.Time min	Peak Name	Height mAU	Area mAU*min	Rel.Area %	Amount	Type
1	7.01	n.a.	663.686	160.704	49.97	n.a.	BMB*
2	14.94	n.a.	281.285	160.885	50.03	n.a.	BMB*
<b>Total:</b>			944.971	321.589	100.00	0.000	



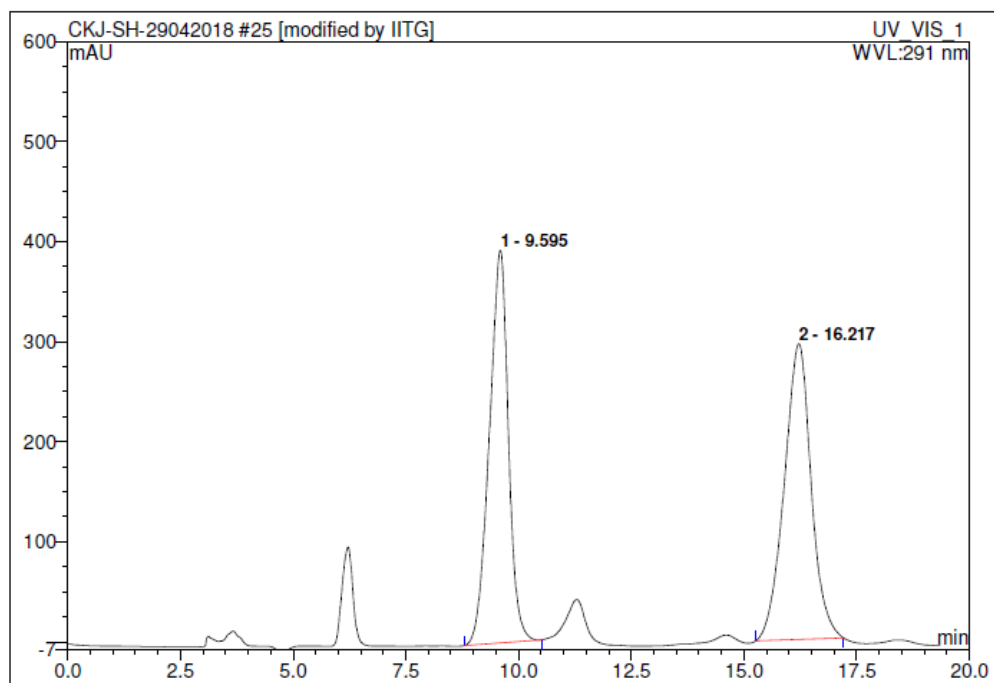
No.	Ret.Time min	Peak Name	Height mAU	Area mAU*min	Rel.Area %	Amount	Type
1	10.81	n.a.	16.970	9.964	4.05	n.a.	BMB*
2	12.82	n.a.	374.773	236.049	95.95	n.a.	BMB*
<b>Total:</b>			391.743	246.014	100.00	0.000	



No.	Ret.Time min	Peak Name	Height mAU	Area mAU*min	Rel.Area %	Amount	Type
1	10.85	n.a.	100.906	65.002	50.72	n.a.	BM *
2	12.69	n.a.	99.098	63.145	49.28	n.a.	MB*
<b>Total:</b>			200.004	128.148	100.00	0.000	



No.	Ret.Time min	Peak Name	Height mAU	Area mAU*min	Rel.Area %	Amount	Type
1	9.54	n.a.	136.610	71.806	98.68	n.a.	BMB*
2	15.77	n.a.	2.221	0.962	1.32	n.a.	BMB*
<b>Total:</b>			138.831	72.768	100.00	0.000	



No.	Ret.Time min	Peak Name	Height mAU	Area mAU*min	Rel.Area %	Amount	Type
1	9.60	n.a.	392.325	191.855	48.42	n.a.	BMB*
2	16.22	n.a.	295.443	204.403	51.58	n.a.	BMB*
<b>Total:</b>			687.768	396.258	100.00	0.000	