Organocatalytic asymmetric Mannich reaction of pyrazoleamides with cyclic trifluoromethyl ketimines: enantioselective access to dihydroquinazolinone skeletons

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Supporting Information

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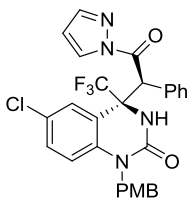
1. General experimental information

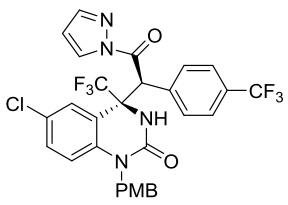
Reagents were purchased from commercial sources and were used as received unless mentioned otherwise. Reactions were monitored by TLC. ^{1}H NMR and ^{13}C NMR spectra were recorded in $CDCl_3$ and DMSO-d_6. ^{1}H NMR chemical shifts are reported in ppm relative to tetramethylsilane (TMS) with the solvent resonance employed as the internal standard ($CDCl_3$ at 7.26 ppm, DMSO-d_6 at 2.50 ppm). Data are reported as follows: chemical shift, multiplicity (s = singlet, br s = broad singlet, d = doublet, t = triplet, q = quartet, m = multiplet), coupling constants (Hz) and integration. ^{13}C NMR chemical shifts are reported in ppm from tetramethylsilane (TMS) with the solvent resonance as the internal standard ($CDCl_3$ at 77.20 ppm, DMSO-d_6 at 39.51 ppm). Melting points were recorded on a melting point apparatus.

2. General experimental procedures for asymmetric synthesis of compounds 3

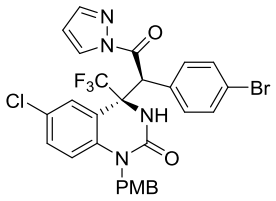
In an ordinary vial equipped with a magnetic stirring bar, pyrazoleamides **1** (0.2 mmol, 2.0 equiv.), trifluoromethyl ketimines **2** (0.1 mmol, 1.0 equiv.) and catalyst **C** (10 mol %, 0.01 mmol) were placed in 0.5 mL of DCM at 30 ℃, and the resulting mixture was stirred at this temperature until the reaction completed (monitored by TLC). The residue was purified by column chromatography (petroleum ether/ethyl acetate = 5/1) to give the desired product **3**.



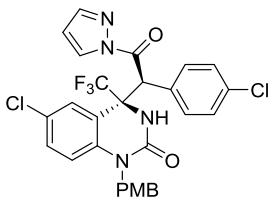
(*S*)-6-chloro-1-(4-methoxybenzyl)-4-((*S*)-2-oxo-1-phenyl-2-(1*H*-pyrazol-1-yl)ethyl)-4-(trifluoromethyl)-3,4-dihydroquinazolin-2(1*H*)-one (3a). White solid; 48.5 mg, 87% yield; >20:1 dr, 99% ee; $[\alpha]_D^{20}$ = - 15.4 (c 1.00, CH_2Cl_2); m.p. 188.1-188.5 ℃; HPLC (AD-H, *i*-propanol/*n*-hexane = 30/70, flow rate = 1.0 mL/min, λ = 254 nm) t_R = 11.5 min (minor), 29.0 min (major); ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.27 (d, *J* = 2.9 Hz, 1H), 7.78 (s, 1H), 7.59 - 7.41 (m, 3H), 7.38 (s, 1H), 7.28 - 7.10 (m, 3H), 7.08 - 6.98 (m, 1H), 6.88 - 6.70 (m, 4H), 6.55 - 6.43 (m, 2H), 6.15 (s, 1H), 4.98 (d, *J* = 16.6 Hz, 1H), 4.81 (d, *J* = 16.6 Hz, 1H), 3.75 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 169.2, 158.6, 151.0, 145.0, 136.8, 130.7, 130.4, 128.8, 128.7, 128.6, 127.7, 127.10, 127.06, 126.88, 126.85, 124.6 (q, *J* = 287.0 Hz), 116.2, 115.5, 114.1, 111.2, 65.7 (q, *J* = 27.8 Hz), 55.2, 49.2, 45.1; HRMS (ESI) calcd. for $C_{28}H_{22}ClF_3N_4NaO_3$ $[M + Na]^+$ 577.1225, found: 577.1258.



(*S*)-6-chloro-1-(4-methoxybenzyl)-4-((*S*)-2-oxo-2-(1*H*-pyrazol-1-yl)-1-(4-(trifluoromethyl)phenyl)ethyl)-4-(trifluoromethyl)-3,4-dihydroquinazolin-2(1*H*)-one (3b). White solid; 51.4 mg, 83% yield; >20:1 dr, 93% ee; $[\alpha]_D^{20}$ = - 3.2 (c 2.57, CH_2Cl_2); m.p. 113.0-113.6 ℃; HPLC (OD-H, *i*-propanol/*n*-hexane = 10/90, flow rate = 1.0 mL/min, λ = 254 nm) t_R = 7.6 min (minor), 8.1 min (major); ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.28 (d, *J* = 2.9 Hz, 1H), 7.80 (s, 1H), 7.64 (d, *J* = 8.2 Hz, 2H), 7.50 (t, *J* = 7.5 Hz, 3H), 7.35 (s, 1H), 7.14 - 7.02 (m, 1H), 6.88 - 6.70 (m, 4H), 6.59 - 6.47 (m, 2H), 6.25 (s, 1H), 5.02 (d, *J* = 16.7 Hz, 1H), 4.81 (d, *J* = 16.5 Hz, 1H), 3.74 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 168.7, 158.8, 150.8, 145.3, 136.8, 135.0, 131.2, 130.77 (q, *J* = 33.0 Hz), 130.79, 128.9, 127.4, 127.3, 127.0, 126.7, 125.5 (q, *J* = 3.8 Hz), 124.5 (q, *J* = 287.3 Hz), 121.8, 116.5, 115.0, 114.1, 111.6, 65.6 (q, *J* = 28.0 Hz), 55.1, 48.9, 45.2; HRMS (ESI) calcd. for $C_{29}H_{22}ClF_6N_4O_3$ $[M + H]^+$ 623.1279, found: 623.1267.

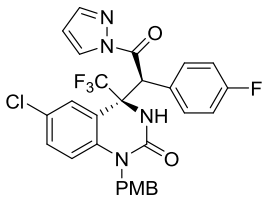


(*S*)-4-((*S*)-1-(4-bromophenyl)-2-oxo-2-(1*H*-pyrazol-1-yl)ethyl)-6-chloro-1-(4-methoxybenzyl)-4-(trifluoromethyl)-3,4-dihydroquinazolin-2(1*H*)-one (3c). White solid; 56.9 mg, 90% yield; >20:1 dr, 98% ee; $[\alpha]_D^{20}$ = - 18.5 (c 2.85, CH_2Cl_2); m.p. 112.1-113.5 ℃; HPLC (AD-H, *i*-propanol/*n*-hexane = 40/60, flow rate = 1.0 mL/min, λ = 254 nm) t_R = 9.9 min (minor), 27.6 min (major); ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.27 (d, *J* = 2.9 Hz, 1H), 7.81 - 7.74 (m, 1H), 7.51 (s, 1H), 7.33 (d, *J* = 14.3 Hz, 5H), 7.14 - 7.01 (m, 1H), 6.91 - 6.71 (m, 4H), 6.58 - 6.46 (m, 2H), 6.12 (s, 1H), 5.13 (d, *J* = 16.7 Hz, 1H), 4.74 (d, *J* = 16.8 Hz, 1H), 3.76 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 168.9, 158.7, 150.8, 145.1, 136.8, 132.3, 131.9, 130.7, 129.9, 128.8, 127.4, 127.2, 127.0, 126.6, 123.2, 124.5 (q, *J* = 287.3 Hz), 116.5, 115.1, 114.2, 111.4, 65.6 (q, *J* = 28.0 Hz), 55.2, 48.8, 45.1; HRMS (ESI) calcd. for $C_{28}H_{22}BrClF_3N_4O_3$ $[M + H]^+$ 633.0510, found: 633.0485.

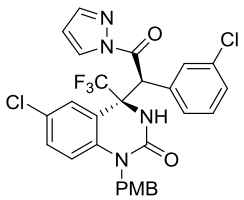


(*S*)-6-chloro-4-((*S*)-1-(4-chlorophenyl)-2-oxo-2-(1*H*-pyrazol-1-yl)ethyl)-1-(4-methoxybenzyl)-4-(trifluoromethyl)-3,4-dihydroquinazolin-2(1*H*)-one (3d). White solid; 29.1 mg, 49% yield; >20:1 dr, 99% ee; $[\alpha]_D^{20}$ = - 20.3 (c 1.45, CH_2Cl_2); m.p. 124.1-124.5 ℃; HPLC (AD-H, *i*-propanol/*n*-hexane = 40/60, flow rate = 1.0 mL/min, λ = 254 nm) t_R = 9.8 min (minor), 22.6 min (major); ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.27 (d, *J* = 2.9 Hz, 1H), 7.78 (d, *J* = 0.9 Hz, 1H), 7.51 (s,

1H), 7.46 - 7.37 (m, 2H), 7.30 (s, 1H), 7.24 - 7.15 (m, 2H), 7.07 (dd, *J* = 8.9, 2.3 Hz, 1H), 6.79 (s, 4H), 6.57 - 6.47 (m, 2H), 6.13 (s, 1H), 5.12 (d, *J* = 16.5 Hz, 1H), 4.75 (d, *J* = 16.7 Hz, 1H), 3.76 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 169.0, 158. 8, 150.8, 145.1, 136.9, 135.0, 132.1, 130.7, 129.4, 128.9, 128.8, 127.5, 127.3, 127.1, 126.7, 124.6 (q, *J* = 287.0 Hz), 116.5, 115.3, 114.2, 111.4, 65.7 (q, *J* = 27.8 Hz), 55.2, 48.8, 45.1; HRMS (ESI) calcd. for $C_{28}H_{22}Cl_2F_3N_4O_3$ $[M + H]^+$ 589.1016, found: 589.0997.

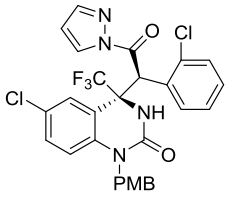


(*S*)-6-chloro-4-((*S*)-1-(4-fluorophenyl)-2-oxo-2-(1*H*-pyrazol-1-yl)ethyl)-1-(4-methoxybenzyl)-4-(trifluoromethyl)-3,4-dihydroquinazolin-2(1*H*)-one (3e). White solid; 40.0 mg, 70% yield; >20:1 dr, 95% ee; $[\alpha]_D^{20}$ = - 17.2 (c 2.00, CH_2Cl_2); m.p. 96.5-96.8 ℃; HPLC (OD-H, *i*-propanol/*n*-hexane = 10/90, flow rate = 1.0 mL/min, λ = 254 nm) t_R = 7.5 min (minor), 8.4 min (major); ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.28 (d, *J* = 2.9 Hz, 1H), 7.78 (d, *J* = 0.8 Hz, 1H), 7.57 - 7.40 (m, 3H), 7.31 (s, 1H), 7.12 - 7.01 (m, 1H), 6.96 - 6.71 (m, 6H), 6.58 - 6.47 (m, 2H), 6.14 (s, 1H), 5.05 (d, *J* = 16.5 Hz, 1H), 4.79 (d, *J* = 16.5 Hz, 1H), 3.75 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 169.2, 162.8 (d, *J* = 248.3 Hz), 158.7, 150.9, 145.1, 136.8, 132.5 (d, *J* = 8.3 Hz), 130.6, 128.8, 127.6, 127.2, 127.1, 126.7, 126.6 (d, *J* = 3.8 Hz), 124.6 (q, *J* = 287.3 Hz), 116.4, 115.7 (d, *J* = 21.8 Hz), 115.4, 114.1, 111.3, 65.7 (q, *J* = 27.8 Hz), 55.1, 48.6, 45.1; HRMS (ESI) calcd. for $C_{28}H_{22}ClF_4N_4O_3$ $[M + H]^+$ 573.1311, found: 573.1290.

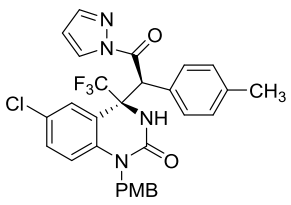


(*S*)-6-chloro-4-((*S*)-1-(3-chlorophenyl)-2-oxo-2-(1*H*-pyrazol-1-yl)ethyl)-1-(4-methoxybenzyl)-4-(trifluoromethyl)-3,4-dihydroquinazolin-2(1*H*)-one (3f). White solid; 49.0 mg, 83% yield; >20:1 dr, 98% ee; $[\alpha]_D^{20}$ = - 18.8 (c 2.45, CH_2Cl_2); m.p. 81.1-82.3 ℃; HPLC (IC, *i*-propanol/*n*-hexane = 30/70, flow rate = 1.0 mL/min, λ = 254 nm) t_R = 6.6 min (major), 7.0 min (minor); ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.32 - 8.24 (m, 1H), 7.83 - 7.76 (m, 1H), 7.58 - 7.45 (m, 2H), 7.41 - 7.31 (m, 2H), 7.24 - 7.01 (m, 3H), 6.90 (d, *J* = 8.8 Hz, 2H), 6.84 - 6.74 (m, 2H), 6.59 - 6.47 (m, 2H), 6.15 (s, 1H), 5.07 (d, *J* = 16.4 Hz, 1H), 4.80 (d, *J* = 16.6 Hz, 1H), 3.75 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 168.8, 158.7, 150.9, 145.2, 136.9, 134.5, 132.8, 130.6, 130.5, 129.7, 129.1, 128.9, 128.8, 127.7, 127.2, 127.1, 126.8, 124.5 (q, *J* = 287.3 Hz), 116.3, 115.2, 114.2, 111.4, 65.5 (q, *J* = 28.5

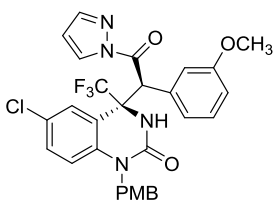
Hz), 55.2, 48.5, 45.3; HRMS (ESI) calcd. for $C_{28}H_{22}Cl_2F_3N_4O_3$ $[M + H]^+$ 589.1016, found: 589.1023.



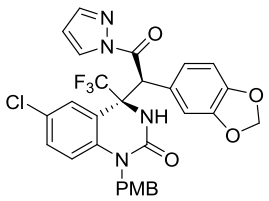
(*S*)-6-chloro-4-((*S*)-1-(2-chlorophenyl)-2-oxo-2-(1*H*-pyrazol-1-yl)ethyl)-1-(4-methoxybenzyl)-4-(trifluoromethyl)-3,4-dihydroquinazolin-2(1*H*)-one (3g). White solid; 23.0 mg, 39% yield; >20:1 dr, 95% ee; $[\alpha]_D^{20}$ = 27.9 (c 1.15, CH_2Cl_2); m.p. 83.4-83.8 ℃; HPLC (AD-H, *i*-propanol/*n*-hexane = 30/70, flow rate = 1.0 mL/min, λ = 254 nm) t_R = 14.2 min (minor), 21.0 min (major); ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.26 (d, *J* = 2.9 Hz, 1H), 8.16 - 8.06 (m, 1H), 7.87 - 7.81 (m, 1H), 7.76 (s, 1H), 7.26 - 7.13 (m, 4H), 7.07 - 7.01 (m, 1H), 6.92 - 6.86 (m, 3H), 6.81 - 6.71 (m, 2H), 6.54 - 6.45 (m, 2H), 4.95 (d, *J* = 16.6 Hz, 1H), 4.86 (d, *J* = 16.4 Hz, 1H), 3.75 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 169.2, 158.7, 151.1, 145.2, 136.3, 135.7, 131.1, 130.7, 130.3, 130.0, 129.2, 128.8, 127.8, 127.4 (q, *J* = 286.7 Hz), 127.28, 127.26, 127.1, 115.8, 114.7, 114.4, 114.2, 111.5, 66.3 (q, *J* = 27.3 Hz), 55.3, 45.3, 44.3; HRMS (ESI) calcd. for $C_{28}H_{22}Cl_2F_3N_4O_3$ $[M + H]^+$ 589.1016, found: 589.1001.



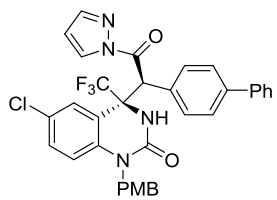
(*S*)-6-chloro-1-(4-methoxybenzyl)-4-((*S*)-2-oxo-2-(1*H*-pyrazol-1-yl)-1-(p-tolyl)ethyl)-4-(trifluoromethyl)-3,4-dihydroquinazolin-2(1*H*)-one (3h). White solid; 54.4 mg, 96% yield; >20:1 dr, 99% ee; $[\alpha]_D^{20}$ = - 11.3 (c 2.72, CH_2Cl_2); m.p. 99.8-100.1 ℃; HPLC (AD-H, *i*-propanol/*n*-hexane = 30/70, flow rate = 1.0 mL/min, λ = 254 nm) t_R = 18.9 min (minor), 23.8 min (major); ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.30 - 8.21 (m, 1H), 7.80 - 7.72 (m, 1H), 7.52 (s, 1H), 7.46 - 7.28 (m, 3H), 7.09 - 6.93 (m, 3H), 6.91 - 6.68 (m, 4H), 6.54 - 6.42 (m, 2H), 6.11 (s, 1H), 5.04 (d, *J* = 16.4 Hz, 1H), 4.80 (d, *J* = 16.5 Hz, 1H), 3.75 (s, 3H), 2.24 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 169.4, 158.6, 151.0, 144.9, 138.5, 136.8, 130.6, 130.3, 129.4, 128.7, 127.74, 127.71, 127.1, 127.0, 126.9, 124.7 (q, *J* = 287.3 Hz), 116.2, 115.6, 114.0, 111.1, 65.6 (q, *J* = 27.8 Hz), 55.1, 48.7, 45.1, 21.1; HRMS (ESI) calcd. for $C_{29}H_{25}ClF_3N_4O_3$ $[M + H]^+$ 569.1562, found: 569.1545.



(*S*)-6-chloro-1-(4-methoxybenzyl)-4-((*S*)-1-(3-methoxyphenyl)-2-oxo-2-(1*H*-pyrazol-1-yl)ethyl)-4-(trifluoromethyl)-3,4-dihydroquinazolin-2(1*H*)-one (3i). White solid; 46.5 mg, 79% yield; >20:1 dr, 98% ee; $[\alpha]_D^{20}$ = - 15.1 (c 2.32, CH_2Cl_2); m.p. 101.2-101.9 ℃; HPLC (AD-H, *i*-propanol/*n*-hexane = 40/60, flow rate = 1.0 mL/min, λ = 254 nm) t_R = 7.7 min (minor), 10.9 min (major); ^{1}H NMR (300 MHz, DMSO-d_6) δ 8.57 (d, *J* = 2.6 Hz, 1H), 8.00 (d, *J* = 1.1 Hz, 1H), 7.81 (s, 1H), 7.60 (s, 1H), 7.27 - 7.13 (m, 2H), 6.97 (d, *J* = 7.3 Hz, 2H), 6.88 (d, *J* = 8.7 Hz, 2H), 6.85 - 6.80 (m, 1H), 6.80 - 6.74 (m, 2H), 6.73 - 6.67 (m, 2H), 6.14 (s, 1H), 5.01 (d, *J* = 17.1 Hz, 1H), 4.83 (d, *J* = 16.3 Hz, 1H), 3.66 (s, 3H), 3.61 (s, 3H); ^{13}C NMR (75 MHz, DMSO-d_6) δ 168.9, 159.0, 158.2, 150.2, 146.0, 136.7, 132.2, 130.6, 129.8, 129.7, 127.9, 127.2, 125.8, 124.6 (q, *J* = 287.3 Hz), 122.5, 116.6, 116.0, 114.7, 114.5, 114.1, 113.9, 112.0, 65.1 (q, *J* = 27.0 Hz), 55.03, 54.99, 49.2, 44.0; HRMS (ESI) calcd. for $C_{29}H_{25}ClF_3N_4O_4$ $[M + H]^+$ 585.1511, found: 585.1494.

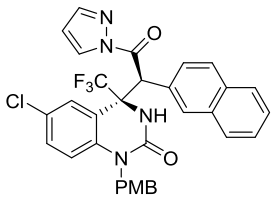


(*S*)-4-((*S*)-1-(benzo[d][1,3]dioxol-5-yl)-2-oxo-2-(1*H*-pyrazol-1-yl)ethyl)-6-chloro-1-(4-methoxybenzyl)-4-(trifluoromethyl)-3,4-dihydroquinazolin-2(1*H*)-one (3j). White solid; 59.0 mg, 99% yield; >20:1 dr, 98% ee; $[\alpha]_D^{20}$ = - 7.0 (c 2.95, CH_2Cl_2); m.p. 97.1-97.8 ℃; HPLC (AD-H, *i*-propanol/*n*-hexane = 40/60, flow rate = 1.0 mL/min, λ = 254 nm) t_R = 10.8 min (minor), 19.8 min (major); ^{1}H NMR (300 MHz, DMSO-d_6) δ 8.55 (d, *J* = 2.7 Hz, 1H), 8.00 (d, *J* = 1.0 Hz, 1H), 7.77 (s, 1H), 7.59 (s, 1H), 7.32 - 7.21 (m, 1H), 7.01 - 6.64 (m, 9H), 6.09 (s, 1H), 5.93 (s, 2H), 5.05 (d, *J* = 16.4 Hz, 1H), 4.86 (d, *J* = 16.6 Hz, 1H), 3.66 (s, 3H); ^{13}C NMR (75 MHz, DMSO-d_6) δ 169.0, 158.3, 150.3, 147.7, 147.4, 146.0, 136.8, 130.6, 129.8, 128.0, 127.4, 127.2, 126.0, 124.4, 124.2, 124.7 (q, *J* = 287.3 Hz), 116.7, 114.8, 113.9, 112.0, 110.3, 108.4, 101.5, 65.1 (q, *J* = 27.0 Hz), 55.0, 48.7, 43.9; HRMS (ESI) calcd. for $C_{29}H_{23}ClF_3N_4O_5$ $[M + H]^+$ 599.1304, found: 599.1283.

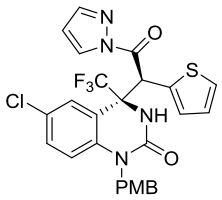


(*S*)-4-((*S*)-1-([1,1'-biphenyl]-4-yl)-2-oxo-2-(1*H*-pyrazol-1-yl)ethyl)-6-chloro-1-(4-methoxybenzyl)-4-(trifluoromethyl)-3,4-dihydroquinazolin-2(1*H*)-one (3k). White solid; 63.0 mg, 99% yield; >20:1 dr, 99% ee; $[\alpha]_D^{20}$ = - 37.1 (c 3.15, CH_2Cl_2); m.p. 168.6-169.2 ℃; HPLC (AD-H, *i*-propanol/*n*-hexane = 40/60, flow rate = 1.0 mL/min, λ = 254 nm) t_R = 12.1 min (minor),

14.2 min (major); ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.31 (d, *J* = 2.9 Hz, 1H), 7.80 (d, *J* = 0.7 Hz, 1H), 7.67 - 7.45 (m, 7H), 7.46 - 7.27 (m, 4H), 7.06 (dd, *J* = 8.9, 2.2 Hz, 1H), 6.76 (d, *J* = 8.6 Hz, 2H), 6.68 - 6.36 (m, 4H), 6.20 (s, 1H), 5.09 (d, *J* = 16.7 Hz, 1H), 4.75 (d, *J* = 16.6 Hz, 1H), 3.49 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 169.2, 158.5, 150.9, 145.0, 141.0, 139.5, 136.9, 131.2, 130.5, 124.6 (q, *J* = 287.0 Hz), 129.7, 128.9, 128.8, 127.7, 127.5, 127.2, 127.0, 126.9, 126.8, 116.4, 115.5, 114.1, 111.2, 65.8 (q, *J* = 28.0 Hz), 54.9, 49.2, 45.1; HRMS (ESI) calcd. for $C_{34}H_{27}ClF_3N_4O_3$ [M + H]$^{+}$ 631.1718, found: 631.1705.

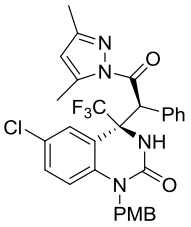


(*S*)-6-chloro-1-(4-methoxybenzyl)-4-((*S*)-1-(naphthalen-2-yl)-2-oxo-2-(1*H*-pyrazol-1-yl)ethyl)-4-(trifluoromethyl)-3,4-dihydroquinazolin-2(1*H*)-one (3l). White solid; 56.4 mg, 93% yield; >20:1 dr, 99% ee; $[\alpha]_D^{20}$ = - 66.2 (c 2.82, CH_2Cl_2); m.p. 101.3-101.5 ℃; HPLC (AD-H, *i*-propanol/*n*-hexane = 40/60, flow rate = 1.0 mL/min, λ = 254 nm) t_R = 11.0 min (minor), 19.7 min (major); ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.29 (d, *J* = 2.5 Hz, 1H), 8.11 (s, 1H), 7.90 - 7.62 (m, 5H), 7.58 - 7.40 (m, 4H), 7.03 - 6.93 (m, 1H), 6.60 - 6.45 (m, 3H), 6.42 - 6.26 (m, 4H), 5.09 (d, *J* = 16.2 Hz, 1H), 4.57 (d, *J* = 16.9 Hz, 1H), 3.64 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 169.2, 158.4, 150.9, 145.0, 136.7, 133.0, 132.8, 130.4, 130.2, 128.8, 128.4, 128.3, 128.2, 127.4, 127.3, 127.1, 126.81, 126.79, 126.76, 126.65, 126.5, 124.7 (q, *J* = 287.3 Hz), 116.3, 115.4, 113.9, 111.2, 65.9 (q, *J* = 27.8 Hz), 55.1, 49.5, 44.9; HRMS (ESI) calcd. for $C_{32}H_{25}ClF_3N_4O_3$ [M + H]$^{+}$ 605.1562, found: 605.1555.

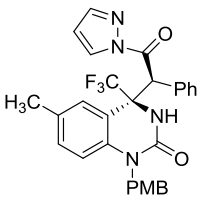


(*S*)-6-chloro-1-(4-methoxybenzyl)-4-((*S*)-2-oxo-2-(1*H*-pyrazol-1-yl)-1-(thiophen-2-yl)ethyl)-4-(trifluoromethyl)-3,4-dihydroquinazolin-2(1*H*)-one (3m). White solid; 53.6 mg, 96% yield; >20:1 dr, 94% ee; $[\alpha]_D^{20}$ = 52.8 (c 2.68, CH_2Cl_2); m.p. 98.1-98.3 ℃; HPLC (AD-H, *i*-propanol/*n*-hexane = 40/60, flow rate = 1.0 mL/min, λ = 254 nm) t_R = 9.1 min (minor), 12.6 min (major); ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.28 (d, *J* = 2.9 Hz, 1H), 7.83 (s, 1H), 7.48 (s, 1H), 7.39 (s, 1H), 7.21 - 7.12 (m, 2H), 7.11 - 7.04 (m, 1H), 6.98 (d, *J* = 8.6 Hz, 2H), 6.88 - 6.75 (m, 3H), 6.67 - 6.49 (m, 3H), 5.11 (d, *J* = 16.2 Hz, 1H), 4.93 (d, *J* = 16.7 Hz, 1H), 3.75 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 168.6, 158.7, 151.0, 145.1, 137.2, 131.9, 130.6, 130.3, 129.0, 127.8, 127.7, 127.3, 127.2, 126.8, 126.6,

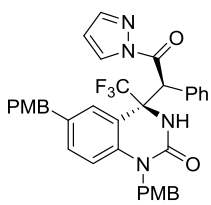
124.6 (q, *J* = 287.3 Hz), 116.3, 115.4, 114.1, 111.6, 65.4 (q, *J* = 27.8 Hz), 55.2, 45.2, 44.6; HRMS (ESI) calcd. for $C_{26}H_{21}ClSF_3N_4O_3$ $[M + H]^+$ 561.0969, found: 561.0975.



(*S*)-6-chloro-4-((*S*)-2-(3,5-dimethyl-1*H*-pyrazol-1-yl)-2-oxo-1-phenylethyl)-1-(4-methoxybenzyl)-4-(trifluoromethyl)-3,4-dihydroquinazolin-2(1*H*)-one (3n). White solid; 10.1 mg, 17% yield; >20:1 dr, 85% ee; $[\alpha]_D^{20}$ = 14.5 (c 0.5, CH_2Cl_2); m.p. 187.8-188.0 ℃; HPLC (AD-H, *i*-propanol/*n*-hexane = 30/70, flow rate = 1.0 mL/min, λ = 254 nm) t_R = 5.7 min (minor), 8.6 min (major); ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.59 (s, 1H), 7.53 - 7.43 (m, 3H), 7.25 - 7.16 (m, 3H), 7.07 - 6.96 (m, 1H), 6.89 - 6.70 (m, 4H), 6.47 (d, *J* = 9.0 Hz, 1H), 6.21 (s, 1H), 5.98 (s, 1H), 4.98 (d, *J* = 16.6 Hz, 1H), 4.83 (d, *J* = 16.6 Hz, 1H), 3.75 (s, 3H), 2.52 (s, 3H), 2.27 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 171.0, 158.7, 153.0, 151.1, 144.6, 137.0, 131.8, 130.9, 130.2, 128.5, 128.2, 127.9, 127.14, 127.09, 126.9, 124.8 (q, *J* = 287.3 Hz), 116.1, 116.0, 114.1, 112.7, 65.7 (q, *J* = 27.8 Hz), 55.2, 49.4, 45.2, 14.6, 13.9; HRMS (ESI) calcd. for $C_{30}H_{27}ClF_3N_4O_3$ $[M + H]^+$ 583.1718, found: 583.1717.

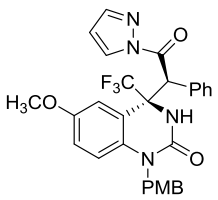


(*S*)-1-(4-methoxybenzyl)-6-methyl-4-((*S*)-2-oxo-1-phenyl-2-(1*H*-pyrazol-1-yl)ethyl)-4-(trifluoromethyl)-3,4-dihydroquinazolin-2(1*H*)-one (3o). White solid; 20.1 mg, 38% yield; >20:1 dr, 99% ee; $[\alpha]_D^{20}$ = 1.9 (c 1.0, CH_2Cl_2); m.p. 189.0-190.2 ℃; HPLC (AD-H, *i*-propanol/*n*-hexane = 30/70, flow rate = 1.0 mL/min, λ = 254 nm) t_R = 9.7 min (minor), 17.0 min (major); ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.33 - 8.18 (m, 1H), 7.93 - 7.64 (m, 1H), 7.50 - 7.40 (m, 2H), 7.35 - 7.28 (m, 2H), 7.22 - 7.12 (m, 3H), 6.92 - 6.78 (m, 3H), 6.78 - 6.68 (m, 2H), 6.53 - 6.39 (m, 2H), 6.18 (s, 1H), 4.97 (d, *J* = 16.4 Hz, 1H), 4.81 (d, *J* = 16.5 Hz, 1H) 3.75 (s, 3H), 2.30 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 169.6, 158.5, 151.5, 144.8, 135.8, 131.3, 131.2, 131.0, 130.8, 128.8, 128.5, 128.4, 128.3, 127.3, 127.2, 125.0 (q, *J* = 287.3 Hz), 114.8, 114.0, 113.9, 111.0, 66.0 (q, *J* = 27.8 Hz), 55.2, 49.5, 45.0, 20.6; HRMS (ESI) calcd. for $C_{29}H_{26}ClF_3N_4O_3$ $[M + H]^+$ 535.1952, found: 535.1962.



(*S*)-1,6-bis(4-methoxybenzyl)-4-((*S*)-2-oxo-1-phenyl-2-(1*H*-pyrazol-1-yl)ethyl)-4-(trifluoromethyl)-3,4-dihydroquinazolin-2(1*H*)-one (3p). White solid; 42.0 mg, 51% yield; >20:1 dr, 98% ee; $[\alpha]_D^{20}$ = 1.0 (c 2.1, CH_2Cl_2); m.p. 99.5-101.0 ℃; HPLC (AD-H, *i*-propanol/*n*-hexane = 30/70, flow rate =

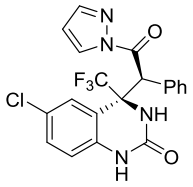
1.0 mL/min, λ = 254 nm) t_R = 10.6 min (minor), 20.1 min (major); ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.27 (d, *J* = 2.9 Hz, 1H), 7.80 - 7.73 (m, 1H), 7.42 - 7.29 (m, 4H), 7.24 - 7.05 (m, 3H), 7.05 - 6.96 (m, 2H), 6.93 - 6.81 (m, 5H), 6.80 - 6.70 (m, 2H), 6.54 - 6.44 (m, 2H), 6.17 (s, 1H), 4.99 (d, *J* = 17.0 Hz, 1H), 4.86 (d, *J* = 16.4 Hz, 1H), 3.86 (s, 2H), 3.80 (s, 3H), 3.75 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 169.6, 158.5, 158.1, 151.4, 144.8, 136.3, 134.9, 132.7, 131.2, 130.83, 130.81, 129.6, 128.7, 128.4, 128.3, 127.49, 127.47, 127.2, 125.0 (q, *J* = 287.3 Hz), 115.0, 114.0, 113.9, 113.8, 111.0, 65.8 (q, *J* = 27.8 Hz), 55.3, 55.2, 48.8, 45.0, 40.0; HRMS (ESI) calcd. for $C_{36}H_{32}ClF_3N_4O_4$ $[M + H]^+$ 641.2370, found: 641.2398.



(*S*)-6-methoxy-1-(4-methoxybenzyl)-4-((*S*)-2-oxo-1-phenyl-2-(1*H*-pyrazol -1-yl)ethyl)-4-(trifluoromethyl)-3,4-dihydroquinazolin-2(1*H*)-one (3q). White solid; 32.5 mg, 59% yield; >20:1 dr, 97% ee; $[\alpha]_D^{20}$ = - 2.9 (c 1.63, CH_2Cl_2); m.p. 96.1-97.0 ℃; HPLC (AD-H, *i*-propanol/*n*-hexane = 30/70, flow rate = 1.0 mL/min, λ = 254 nm) t_R = 10.7 min (minor), 13.7 min (major); ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.27 (d, *J* = 2.9 Hz, 1H), 7.78 - 7.71 (m, 1H), 7.52 - 7.47 (m, 2H), 7.33 - 7.29 (m, 1H), 7.22 - 7.11 (m, 4H), 6.84 (d, *J* = 8.7 Hz, 2H), 6.79 - 6.69 (m, 2H), 6.69 - 6.58 (m, 1H), 6.52 - 6.43 (m, 2H), 6.19 (s, 1H), 4.95 (d, *J* = 16.4 Hz, 1H), 4.81 (d, *J* = 16.8 Hz, 1H), 3.76 (s, 3H), 3.75 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 169.4, 158.5, 154.3, 151.4, 144.7, 131.8, 131.2, 130.8, 129.3, 128.7, 128.5, 128.4, 127.2, 124.9 (q, *J* = 287.3 Hz), 115.8, 115.2, 114.0, 113.41, 113.39, 111.0, 65.9 (q, *J* = 27.5 Hz), 55.7, 55.2, 49.4, 45.1; HRMS (ESI) calcd. for $C_{29}H_{26}ClF_3N_4O_4$ $[M + H]^+$ 551.1901, found: 551.1902.

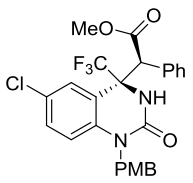
3. Synthesis of compounds 4-8

To compound **3a** (100.0 mg, 0.18 mmol) in a mixture of 1.8 mL acetonitrile and 0.2 mL H_2O was added ammonium cerium(IV) nitrate (200.0 mg, 0.36 mmol) at 0 ℃. After the reaction was stirred for 1 h at 0 ℃, the resulting mixture was warmed to 25 ℃ and stirred for 12 h. The resulting mixture was then poured into aq HCl (1 N), and extracted with DCM three times. The combined organic layers were dried over with Na_2SO_4. After evaporation of solvent, product **4** was purified by flash chromatography on silica gel (petroleum ether/ethyl acetate = 5:1).



(*S*)-6-chloro-4-((*S*)-2-oxo-1-phenyl-2-(1*H*-pyrazol-1-yl)ethyl)-4-(trifluoromethyl)-3,4-dihydroquinazolin-2(1*H*)-one (4). White solid; 39.0 mg, 50% yield; >20:1 dr, 99% ee; $[\alpha]_D^{20}$ = 16.7 (c 1.95, CH_2Cl_2); m.p. 133.3-133.5 ℃; HPLC (AD-H, *i*-propanol/*n*-hexane = 30/70, flow rate = 1.0 mL/min, λ = 254 nm) t_R = 5.9 min (minor), 6.5 min (major); ^{1}H NMR (300 MHz, $CDCl_3$) δ 9.52 (s, 1H), 8.25 (d, *J* = 2.9 Hz, 1H), 7.81 - 7.74 (m, 1H), 7.51 - 7.40 (m, 3H), 7.33 - 7.28 (m, 1H), 7.21 - 7.10 (m, 4H), 6.61 (d, *J* = 8.6 Hz, 1H), 6.52 - 6.44 (m, 1H), 6.15 (s, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 169.4, 152.2, 145.0, 135.7, 130.8, 130.6, 128.8, 128.68, 128.66, 127.2, 126.84, 126.82, 124.7 (q, *J* = 286.9 Hz), 116.7, 113.6, 111.2, 66.6 (q, *J* = 27.8 Hz), 48.7; HRMS (ESI) calcd. for $C_{20}H_{14}ClF_3N_4NaO_2$ $[M + Na]^+$ 457.0650, found: 457.0643.

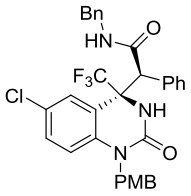
Compound **3a** (277.4 mg, 0.5 mmol) and DBU (30.6 mg, 0.12 mmol) in 3 mL methanol was stirred for 12 h at room temperature. The resulting mixture was concentrated and the residue was purified by flash chromatography on silica gel (petroleum ether/ethyl acetate = 5:1) to give product **5**.



methyl(*S*)-2-((*S*)-6-chloro-1-(4-methoxybenzyl)-2-oxo-4-(trifluoromethyl)-1,2,3,4-tetrahydroquinazolin-4-yl)-2-phenylacetate (5). White solid; 208.2 mg, 80% yield; >20:1 dr, 99% ee; $[\alpha]_D^{20}$ = - 10.5 (c 1.00, CH_2Cl_2); m.p. 110.5-111.0 ℃; HPLC (AD-H, *i*-propanol/*n*-hexane = 30/70, flow rate = 1.0 mL/min, λ = 254 nm) t_R = 9.5 min (minor), 17.3 min (major); ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.44 - 7.32 (m, 3H), 7.27 (s, 1H), 7.25 - 7.15 (m, 3H), 7.03 - 6.93 (m, 1H), 6.76 (q, *J* = 8.8 Hz, 4H), 6.45 (d, *J* = 9.0 Hz, 1H), 4.99 (d, *J* = 16.4 Hz, 1H), 4.77 (d, *J* = 16.5 Hz, 1H), 4.42 (s, 1H), 3.72 (s, 3H), 3.72 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 170.9, 158.5, 150.7, 136.6, 131.1, 130.1, 130.0, 128.4, 128.3, 127.5, 126.9, 126.8, 126.5, 124.4 (q, *J* = 287.3 Hz), 116.1, 115.2, 113.9, 64.9 (q, *J* = 27.8 Hz), 54.9, 52.8, 52.6, 44.9; HRMS (ESI) calcd. for $C_{26}H_{23}ClF_3N_2O_4$ $[M + H]^+$ 519.1293, found: 519.1290.

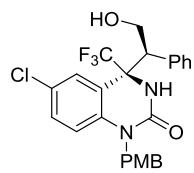
To compound **3a** (55.4 mg, 0.1 mmol) and benzylamine (21.4 mg, 0.2mmol) in 0.5 mL tetrahydrofuran was added DBU (5.4 mg), and then stirred for 12 h at room temperature. The resulting mixture was concentrated and the residue was purified by flash chromatography on silica

gel (petroleum ether/ethyl acetate = 5:1) to give product **6**.



(*S*)-N-benzyl-2-((*S*)-6-chloro-1-(4-methoxybenzyl)-2-oxo-4-(trifluoromethyl)-1,2,3,4-tetrahydroquinazolin-4-yl)-2-phenylacetamide (6). White solid; 30.0 mg, 51% yield; >20:1 dr, 99% ee; $[\alpha]_D^{20}$ = - 39.6 (c 1.50, CH_2Cl_2); m.p. 101.2-101.9 ℃; HPLC (AD-H, *i*-propanol/*n*-hexane = 30/70, flow rate = 1.0 mL/min, λ = 254 nm) t_R = 8.2 min (minor), 16.4 min (major); ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.08 (s, 1H), 7.43 - 7.37 (m, 2H), 7.36 - 7.26 (m, 4H), 7.25 - 7.20 (m, 2H), 7.20 - 7.15 (m, 3H), 7.01 - 6.95 (m, 1H), 6.79 - 6.69 (m, 4H), 6.48 (t, 1H), 6.42 (d, *J* = 9.0 Hz, 1H), 4.95 (d, *J* = 16.7 Hz, 1H), 4.71 (d, *J* = 16.5 Hz, 1H), 4.58 (dd, *J* = 14.8, 6.1 Hz, 1H), 4.27 (dd, *J* = 14.8, 5.0 Hz, 1H), 4.08 (s, 1H), 3.74 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 169.8, 158.6, 151.1, 137.3, 136.9, 132.6, 130.1, 128.7, 128.5, 128.2, 127.9, 127.7, 127.6, 127.1, 126.8, 126.5, 124.8 (q, *J* = 287.3 Hz), 116.2, 114.1, 65.7 (q, *J* = 27.8 Hz), 55.2, 53.6, 45.0, 43.8; HRMS (ESI) calcd. for $C_{32}H_{27}ClF_3N_3NaO_3$ $[M + Na]^+$ 616.1585, found: 616.1595.

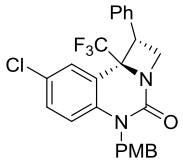
In an ordinary vial equipped with a magnetic stirring bar were added **3a** (100.0 mg, 0.18 mmol, 1 equiv),THF (1.6 mL) and deionized H_2O (0.4 mL). The vial was cooled to 0 ℃ via an icewater bath and stirred for five minutes. After this time, $NaBH_4$ (54.5 mg, 1.44 mmol, 8 equiv) was added slowly portion-wise over few minutes. The reaction was then allowed to stir for 12 h at room temperature. After this time, the reaction was cooled to 0 ℃ via an ice-water bath and quenched with aqueous 1 M HCl carefully, transferred to a separatory funnel, and the organic layers were separated. The aqueous phase was extracted with DCM three times, and the combined organic phase was washed with brine and dried over with Na_2SO_4. The resulting mixture was concentrated and the residue was purified by flash chromatography on silica gel (petroleum ether/ethyl acetate = 5:1) to give the product **7**.



(*S*)-6-chloro-4-((*S*)-2-hydroxy-1-phenylethyl)-1-(4-methoxybenzyl)-4-(trifluoromethyl)-3,4-dihydroquinazolin-2(1*H*)-one (7). White solid; 79.7 mg, 90% yield; >20:1 dr, 99% ee; $[\alpha]_D^{20}$ = - 13.6 (c 3.99, CH_2Cl_2); m.p. 202.0-202.5 ℃; HPLC (AD-H, *i*-propanol/*n*-hexane = 30/70, flow rate = 1.0 mL/min, λ = 254 nm) t_R = 6.9 min (minor), 8.0 min (major); ^{1}H NMR (300 MHz, DMSO-d_6) δ

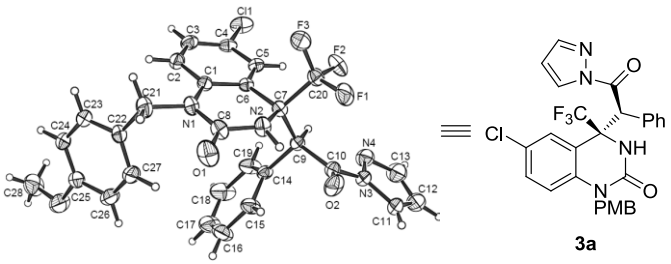
8.13 (s, 1H), 7.64 (s, 1H), 7.28 - 7.09 (m, 6H), 6.81 - 6.67 (m, 4H), 6.52 (d, *J* = 9.0 Hz, 1H), 5.18 (d, *J* = 4.1 Hz, 1H), 4.96 (d, *J* = 16.4 Hz, 1H), 4.67 (d, *J* = 16.7 Hz, 1H), 4.36 - 4.18 (m, 1H), 3.98 (d, *J* = 10.9 Hz, 1H), 3.87 - 3.78 (m, 1H), 3.69 (s, 3H); ^{13}C NMR (75 MHz, DMSO-d_6) δ 158.0, 150.6, 138.1, 136.3, 130.3, 129.5, 128.1, 127.5, 127.0, 126.7, 126.6, 125.4, 125.3 (q, *J* = 287.3 Hz), 118.0, 116.0, 113.8, 65.5 (q, *J* = 26.5 Hz), 61.1, 54.9, 51.2, 43.6; HRMS (ESI) calcd. for $C_{25}H_{23}ClF_3N_2O_3$ $[M + H]^+$ 491.1344, found: 491.1363.

To a suspension of powdered KOH (36.4 mg, 0.65 mmol) in dry THF (2 mL), TsCl (61.8 mg, 0.33 mmol) was added. To this mixture compound **7** (79.7 mg, 0.16 mmol) was added. The mixture was refluxed for 7 h. Cold water was added to the mixture and it was extracted with DCM three times. The extract was washed with water and brine, dried over with anhydrous Na_2SO_4 and concentrated under reduced pressure. The crude product was subjected to column chromatography on silica gel (petroleum ether/ethyl acetate = 5:1) to obtain **8**.



(1*S*,9b*S*)-8-chloro-5-(4-methoxybenzyl)-1-phenyl-9b-(trifluoromethyl)-1,2,5,9b-tetrahydro-4*H*-azeto[1,2-c]quinazolin-4-one (8). White solid; 55.4 mg, 72% yield; >20:1 dr, 98% ee; $[\alpha]_D^{20}$ = 54.6 (c 2.77, CH_2Cl_2); m.p. 80.0-81.0 ℃; HPLC (AD-H, *i*-propanol/*n*-hexane = 30/70, flow rate = 0.8 mL/min, λ = 254 nm) t_R = 8.6 min (minor), 10.6 min (major); ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.32 - 7.24 (m, 3H), 7.21 - 7.06 (m, 4H), 7.02 - 6.92 (m, 1H), 6.91 - 6.79 (m, 2H), 6.64 (d, *J* = 8.9 Hz, 1H), 6.17 - 6.10 (m, 1H), 5.39 (d, *J* = 16.5 Hz, 1H), 4.85 - 4.66 (m, 2H), 4.45 - 4.32 (m, 2H), 3.77 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 158.8, 154.6, 138.8, 134.9, 129.7, 128.8, 128.5, 128.3, 128.1, 127.6, 127.0, 125.1 (q, *J* = 283.5 Hz), 116.1, 115.8, 114.2, 72.9 (q, *J* = 30.5 Hz), 56.7, 55.2, 46.7, 45.6; HRMS (ESI) calcd. for $C_{25}H_{21}ClF_3N_2O_2$ $[M + H]^+$ 473.1238, found: 473.1236.

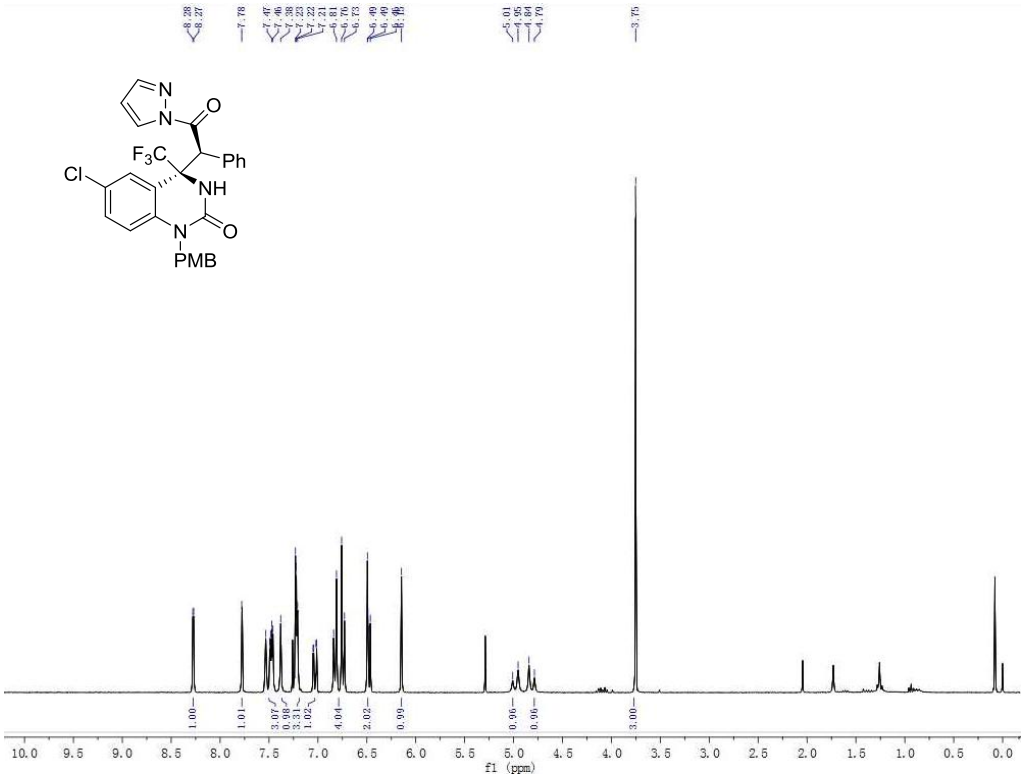
4. X-ray crystallography of compound 3a

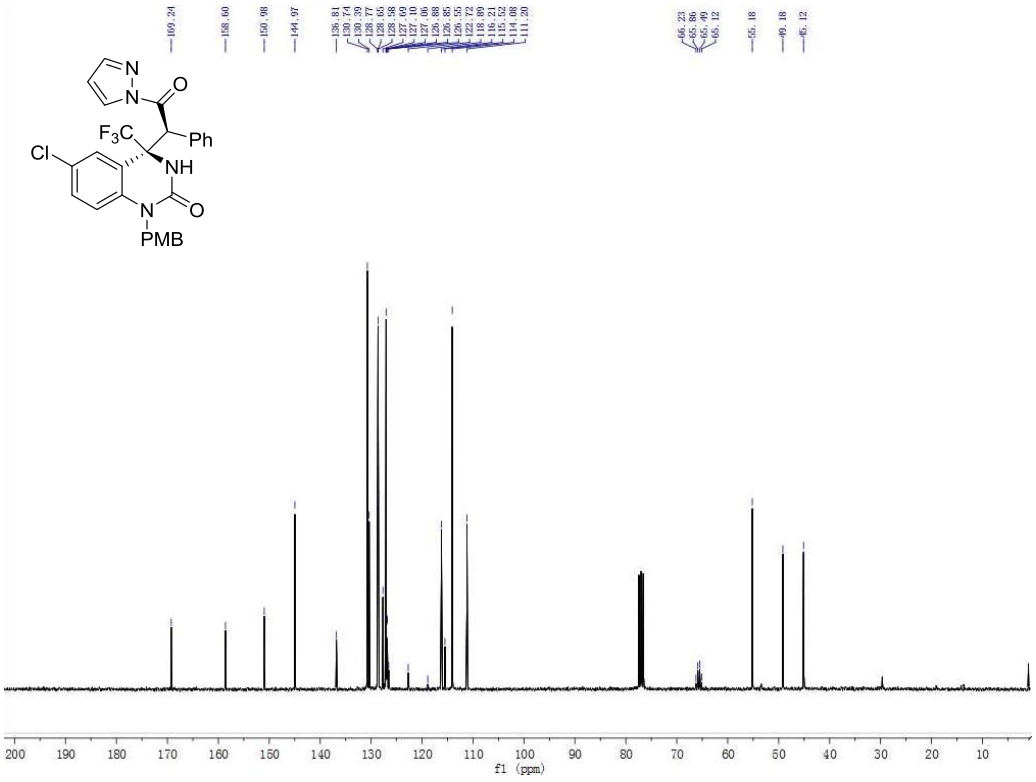


Identification code	**3a** (CCDC 1538899)
Empirical formula	C28H22ClF3N4O3
Formula weight	554.94
Temperature/K	290(2)
Crystal system	orthorhombic
Space group	P212121
a/Å	10.3289(3)
b/Å	13.7520(4)
c/Å	18.4669(7)
α/°	90
β/°	90
γ/°	90
Volume/Å^3	2623.09(15)
Z	4
ρ_{calc}g/cm^3	1.405
μ/mm^{-1}	0.205
F(000)	1144.0
Crystal size/mm^3	0.220 × 0.200 × 0.150
Radiation	MoKα (λ = 0.71073)
2Θ range for data collection/°	6.618 to 59.098
Index ranges	-13 ≤ h ≤ 14, -17 ≤ k ≤ 17, -24 ≤ l ≤ 19
Reflections collected	23974
Independent reflections	6528 [Rint = 0.0282, Rsigma = 0.0277]
Data/restraints/parameters	6528/0/357
Goodness-of-fit on F^2	1.033
Final R indexes [I>=2σ (I)]	R1 = 0.0431, wR2 = 0.0942
Final R indexes [all data]	R1 = 0.0640, wR2 = 0.1040
Largest diff. peak/hole / e Å^{-3}	0.14/-0.21
Flack parameter	0.003(22)

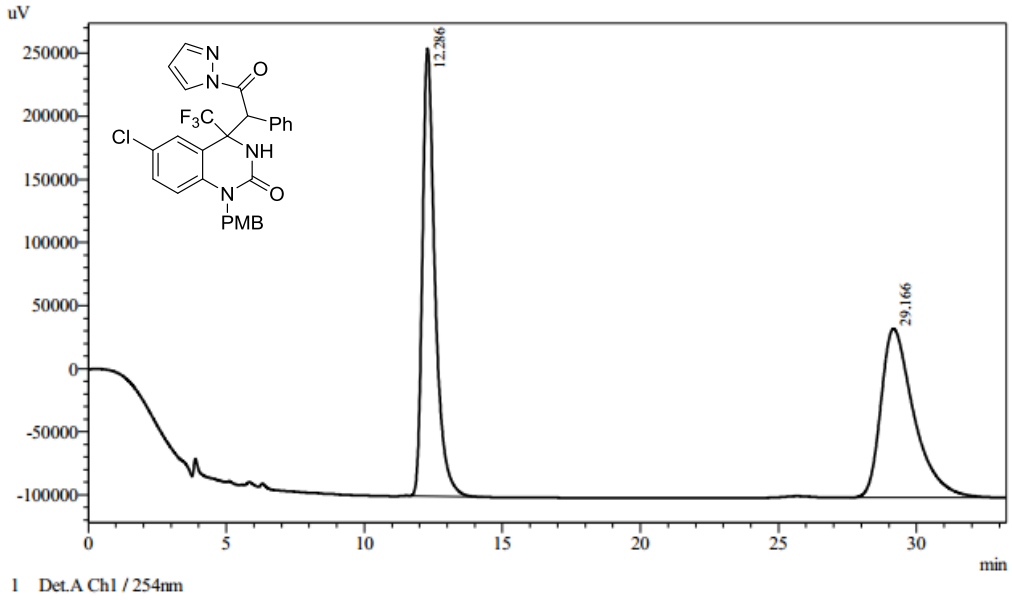
5. ^{1}H, ^{13}C NMR, and HPLC spectra for compounds 3a-q, and compounds 4-8

^{1}H and ^{13}C NMR of **3a**





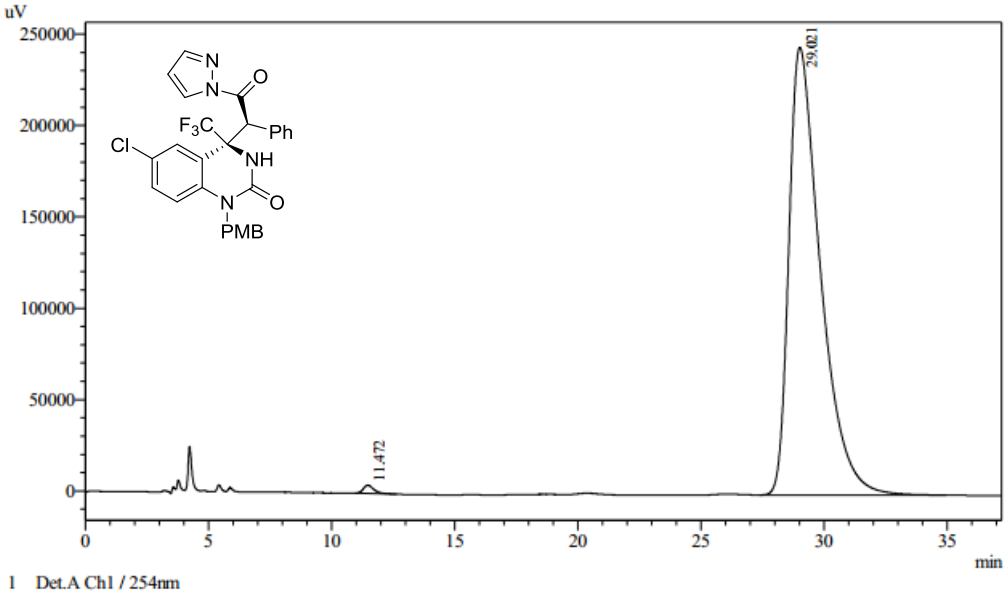
HPLC of **3a**



1 Det.A Ch1 / 254nm

Detector A Ch1 254nm

Peak#	Ret. Time	Area	Height	Area %	Height %
1	12.286	11252305	354794	50.254	72.616
2	29.166	11138480	133798	49.746	27.384
Total		22390784	488592	100.000	100.000

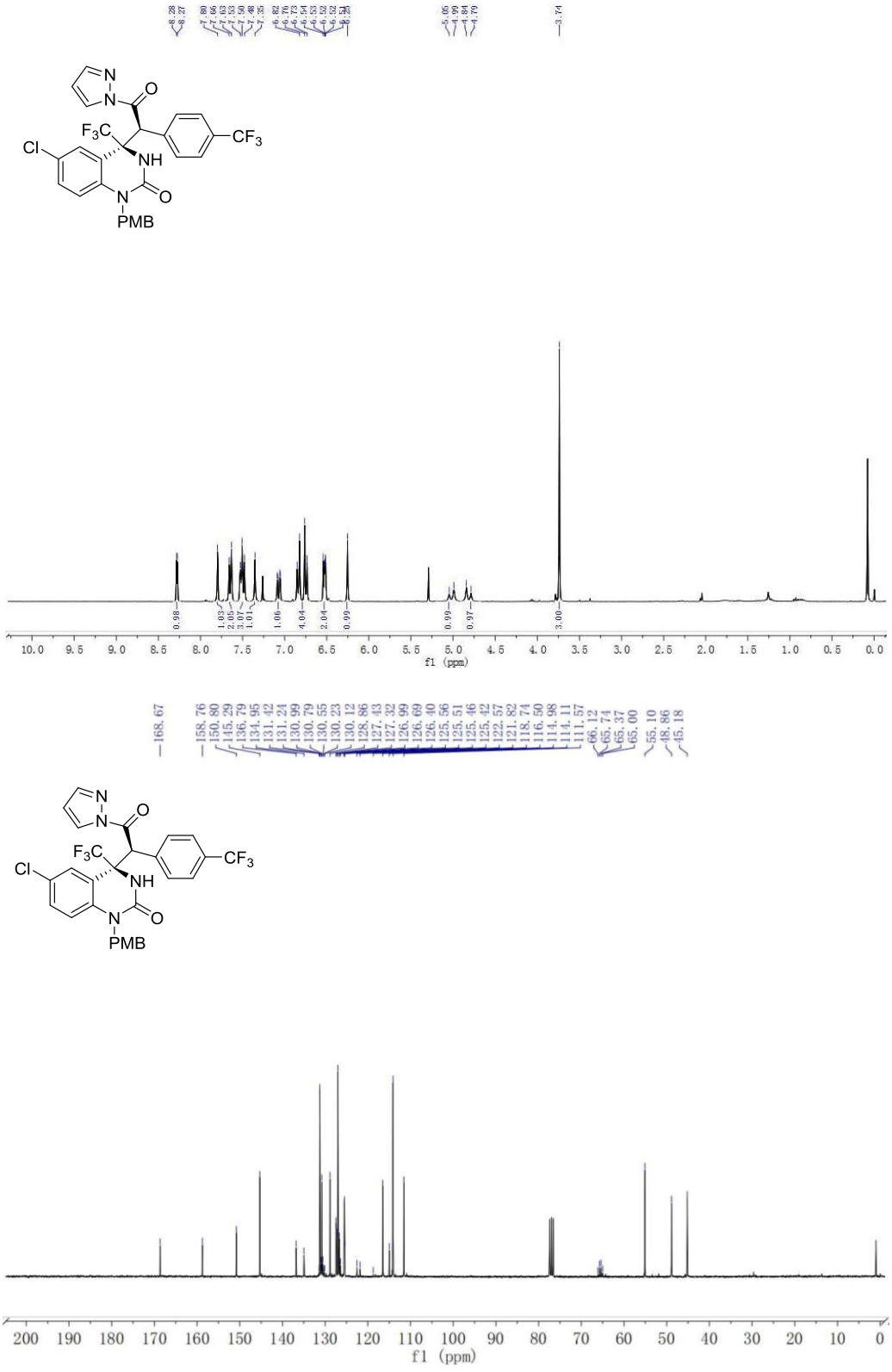


1 Det.A Ch1 / 254nm

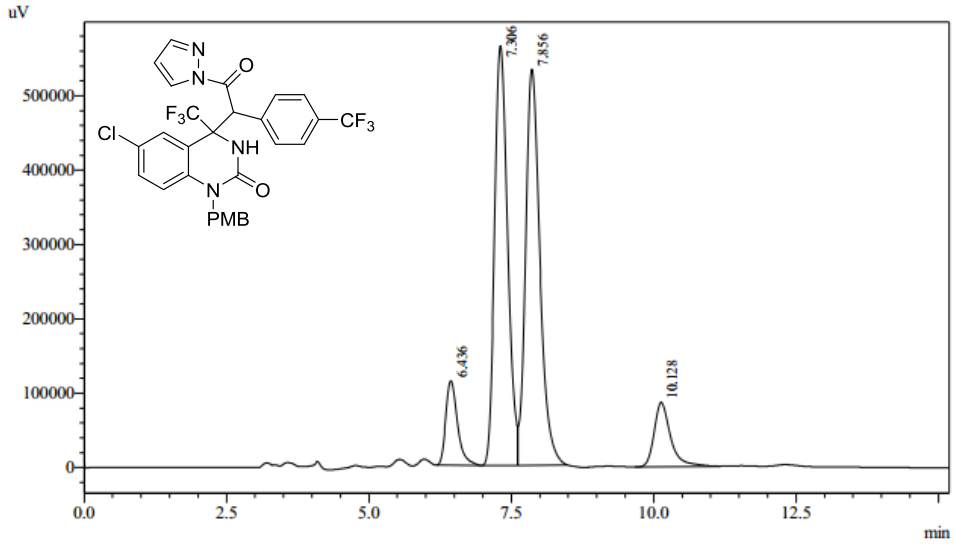
Detector A Ch1 254nm

Peak#	Ret. Time	Area	Height	Area %	Height %
1	11.472	138435	4564	0.630	1.829
2	29.021	21844401	245008	99.370	98.171
Total		21982836	249572	100.000	100.000

^{1}H and ^{13}C NMR of **3b**



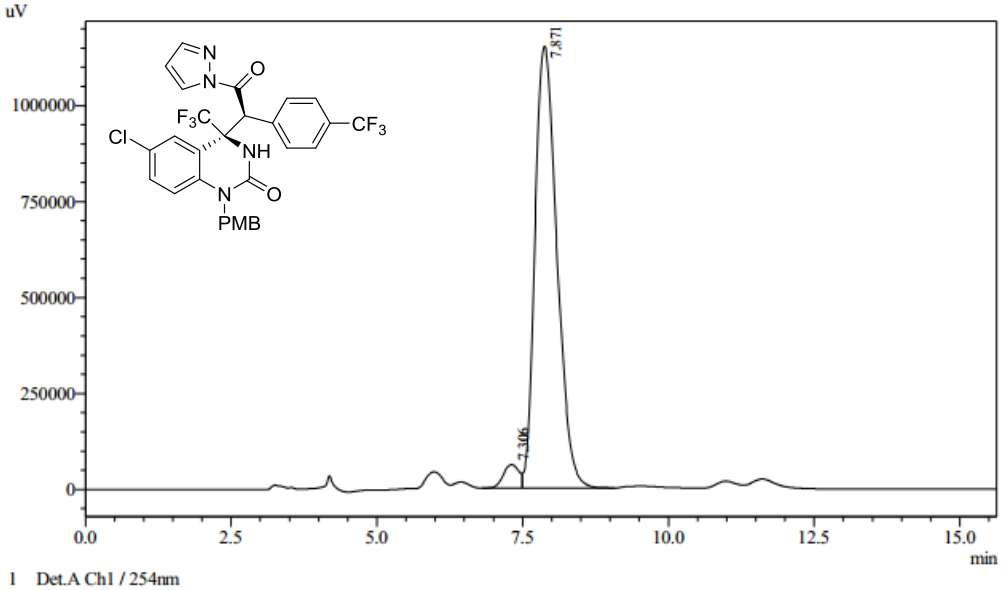
HPLC of **3b**



1 Det.A Ch1 / 254nm

Detector A Ch1 254nm

Peak#	Ret. Time	Area	Height	Area %	Height %
1	6.436	1635805	113771	7.582	8.767
2	7.306	8943985	564359	41.458	43.488
3	7.856	9248574	532789	42.870	41.056
4	10.128	1745390	86810	8.090	6.689
Total		21573755	1297729	100.000	100.000

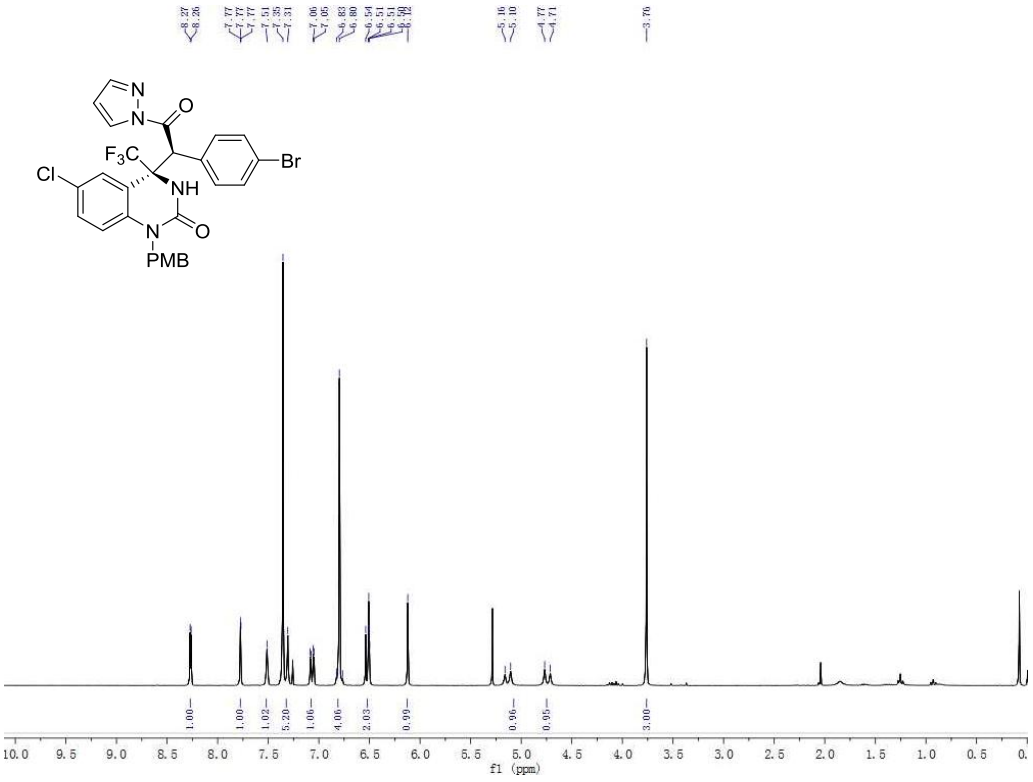


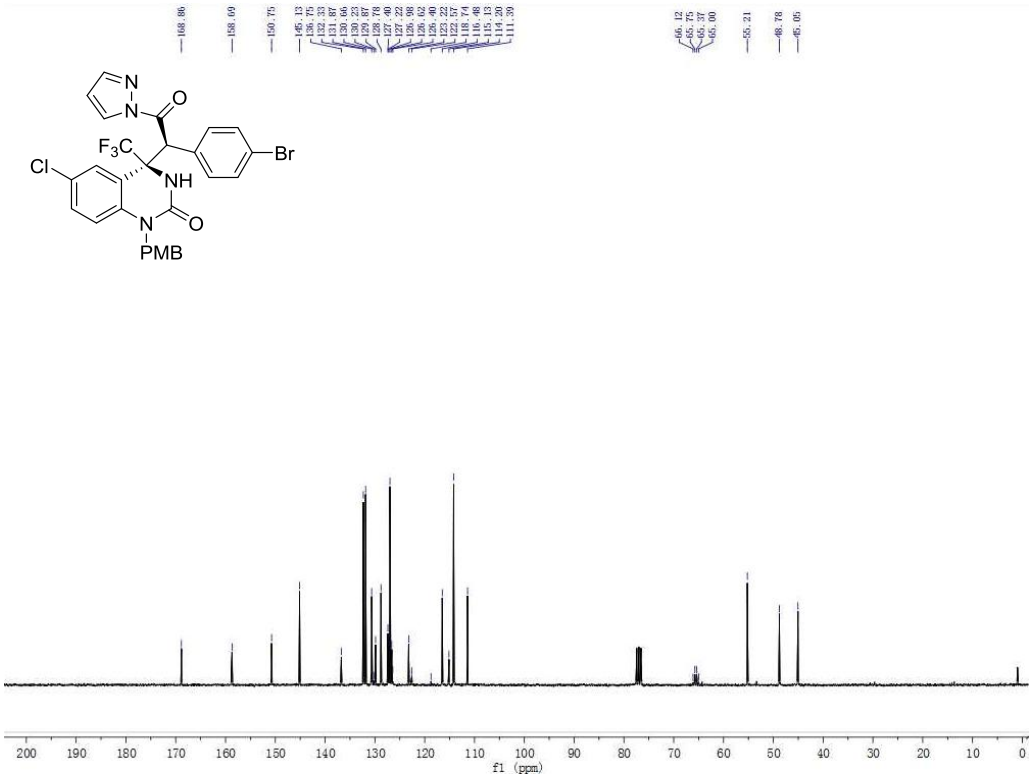
1 Det.A Ch1 / 254nm

Detector A Ch1 254nm

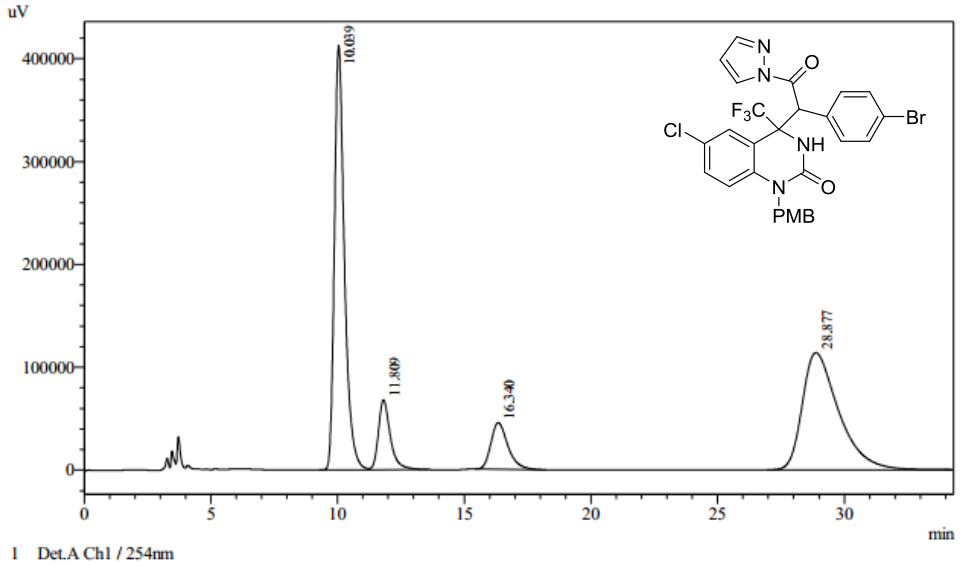
Peak#	Ret. Time	Area	Height	Area %	Height %
1	7.306	1164652	61110	3.725	5.040
2	7.871	30098299	1151467	96.275	94.960
Total		31262950	1212577	100.000	100.000

^{1}H and ^{13}C NMR of **3c**





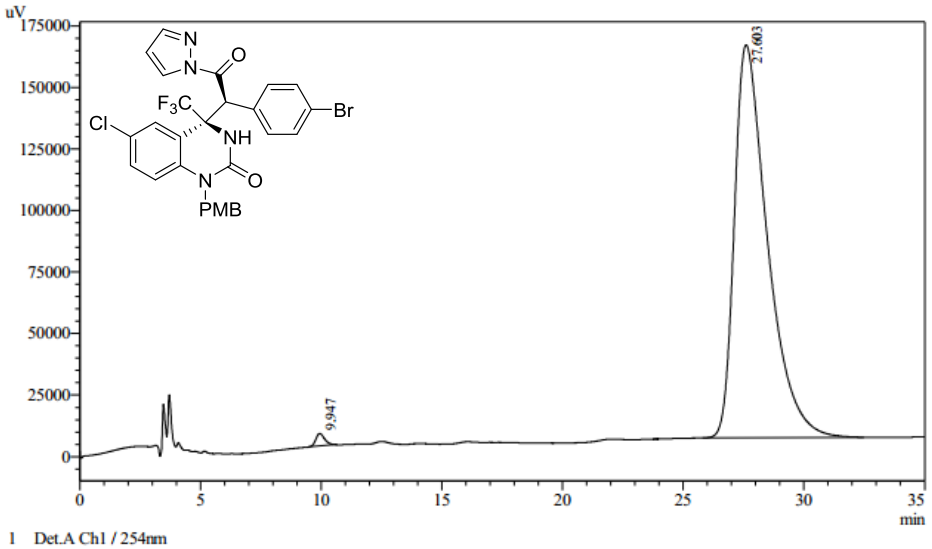
HPLC of **3c**



1 Det.A Ch1 / 254nm

Detector A Ch1 254nm

Peak#	Ret. Time	Area	Height	Area %	Height %
1	10.039	11343952	412765	41.871	64.487
2	11.809	2231904	67965	8.238	10.618
3	16.340	2127715	45417	7.854	7.096
4	28.877	11388956	113925	42.037	17.799
Total		27092526	640073	100.000	100.000

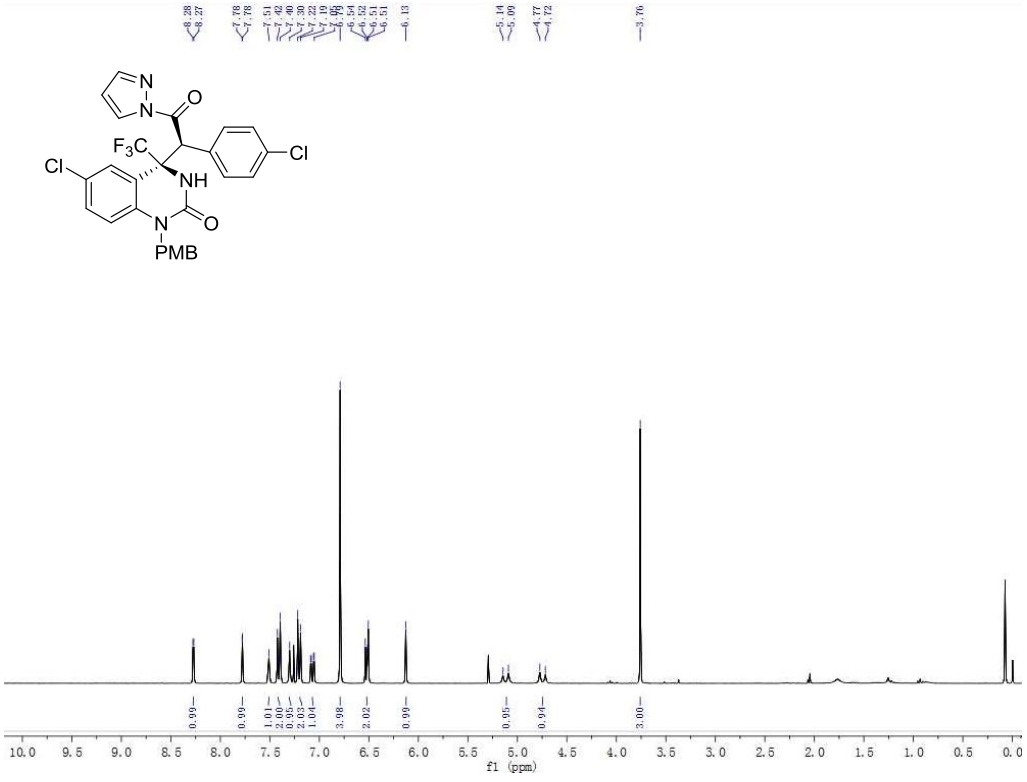


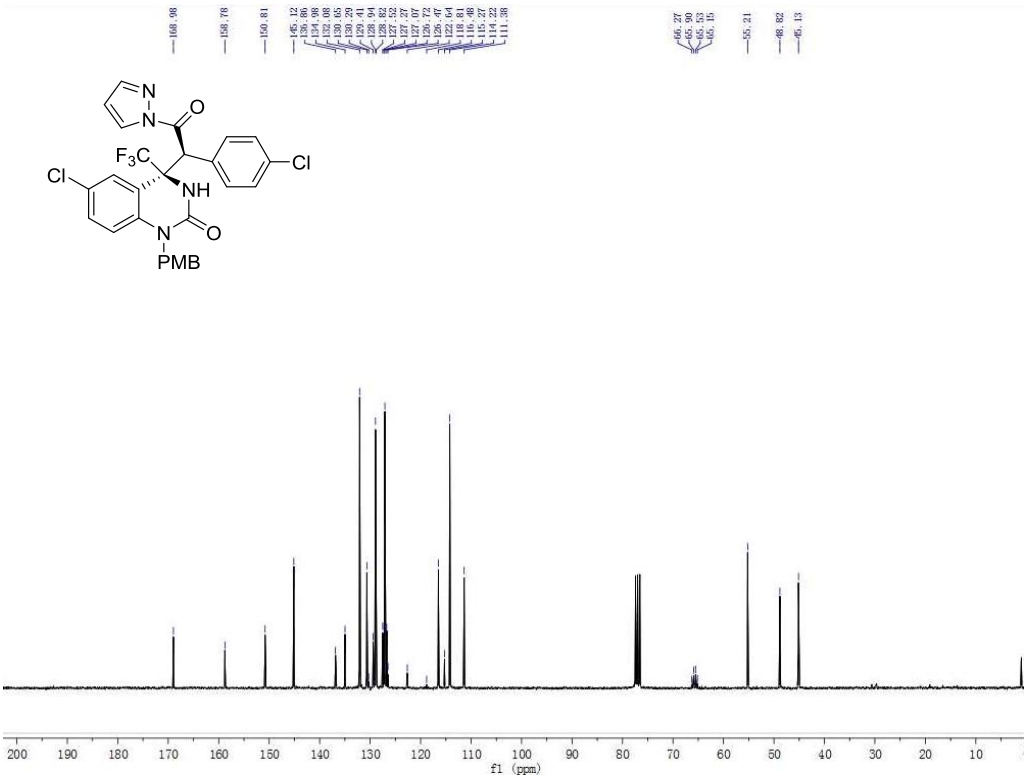
1 Det.A Ch1 / 254nm

Detector A Ch1 254nm

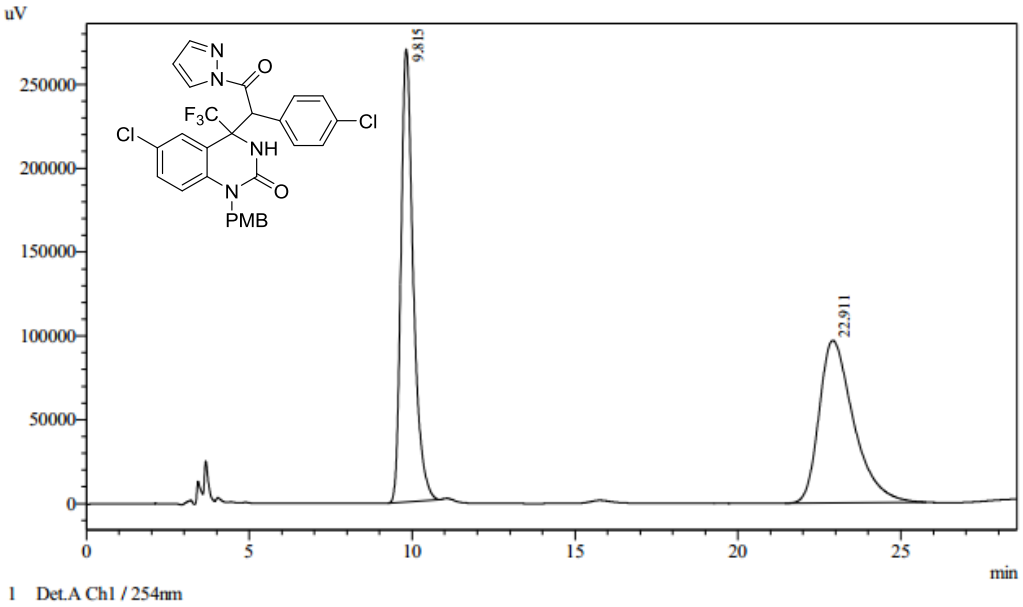
Peak#	Ret. Time	Area	Height	Area %	Height %
1	9.947	130987	5116	0.853	3.105
2	27.603	15224032	159624	99.147	96.895
Total		15355019	164740	100.000	100.000

^{1}H and ^{13}C NMR of **3d**





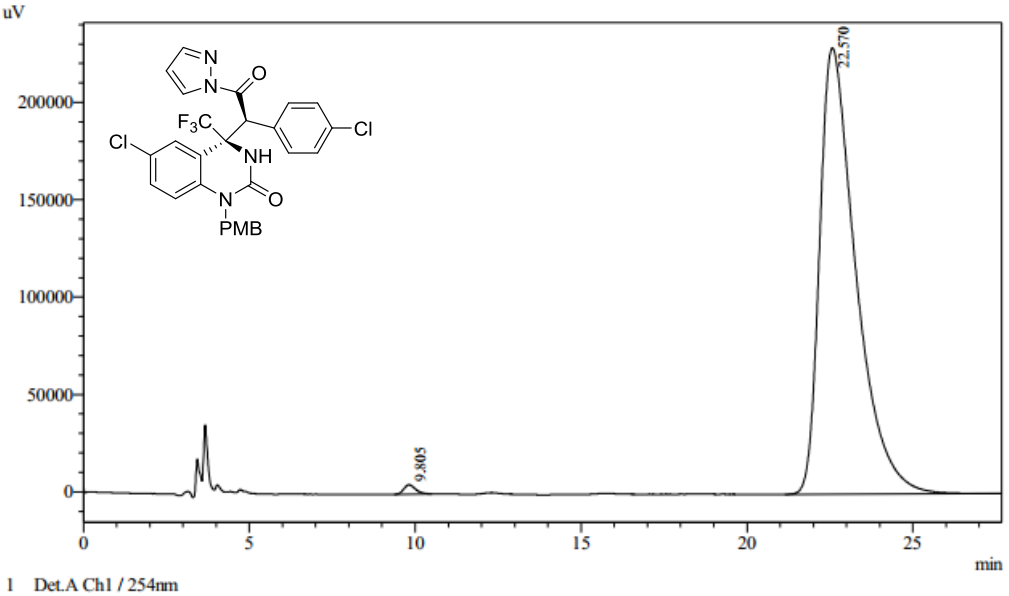
HPLC of **3d**



1 Det.A Ch1 / 254nm

Detector A Ch1 254nm

Peak#	Ret. Time	Area	Height	Area %	Height %
1	9.815	7094612	270114	49.811	73.586
2	22.911	7148345	96959	50.189	26.414
Total		14242958	367073	100.000	100.000

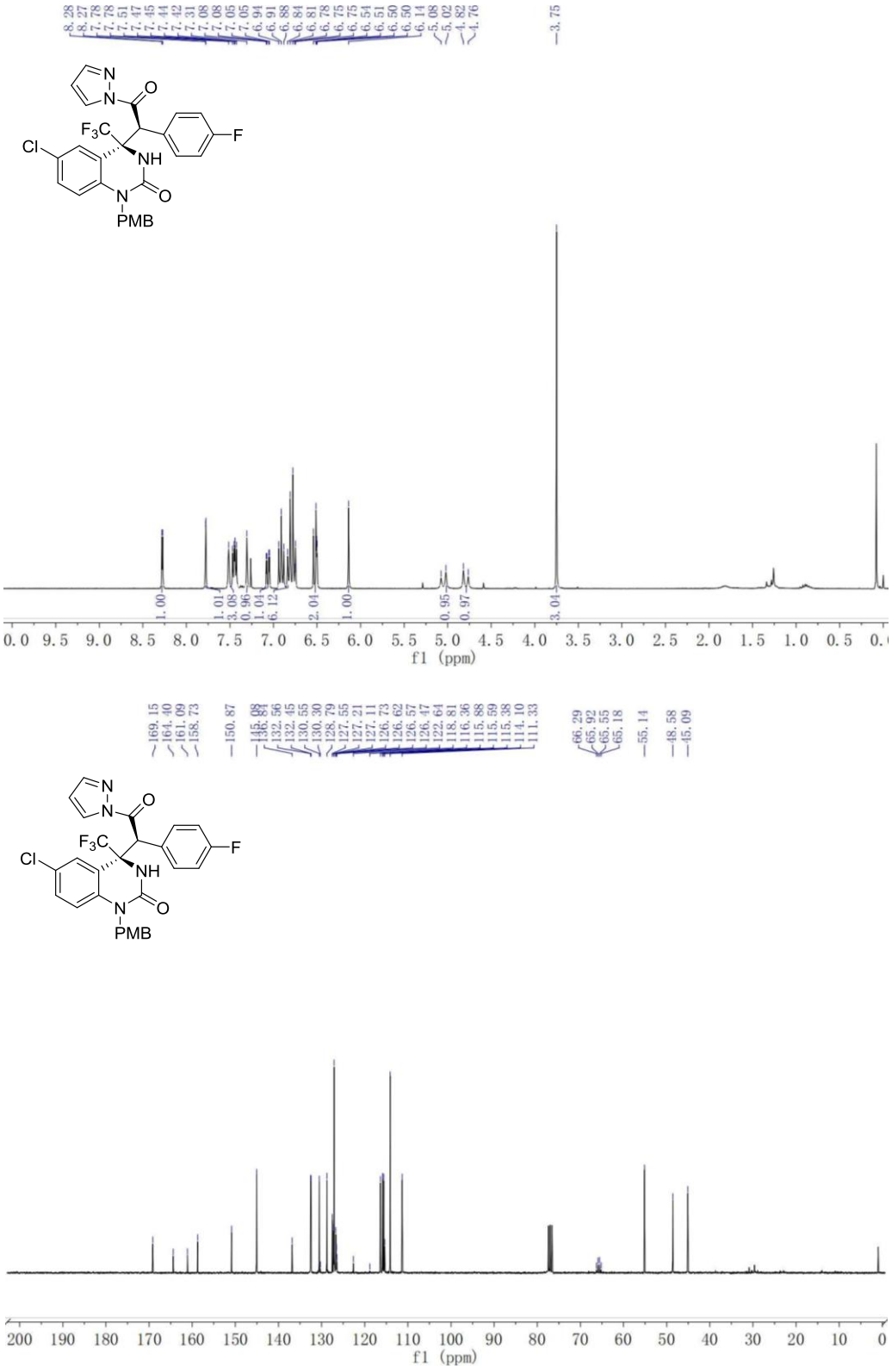


1 Det.A Ch1 / 254nm

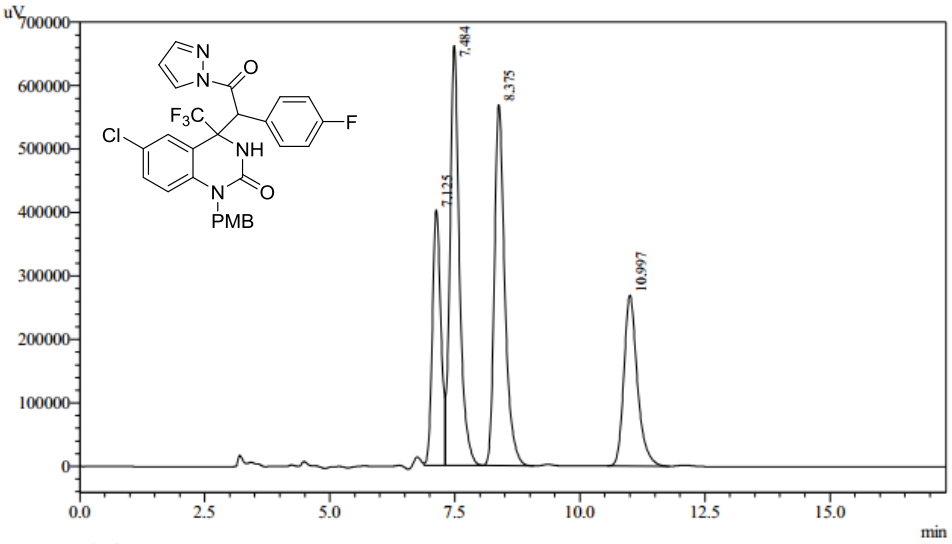
Detector A Ch1 254nm

Peak#	Ret. Time	Area	Height	Area %	Height %
1	9.805	122976	4932	0.701	2.106
2	22.570	17420342	229267	99.299	97.894
Total		17543317	234199	100.000	100.000

^{1}H and ^{13}C NMR of **3e**



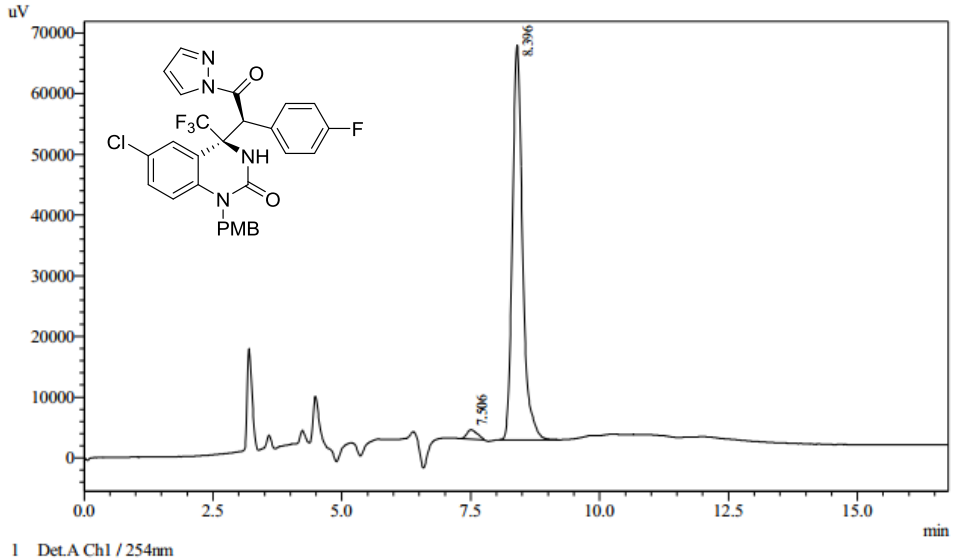
HPLC of **3e**



1 Det.A Ch1 / 254nm

Detector A Ch1 254nm

Peak#	Ret. Time	Area	Height	Area %	Height %
1	7.125	4773181	402728	17.788	21.175
2	7.484	8710820	661244	32.462	34.767
3	8.375	8272756	568449	30.830	29.888
4	10.997	5077052	269499	18.920	14.170
Total		26833808	1901920	100.000	100.000

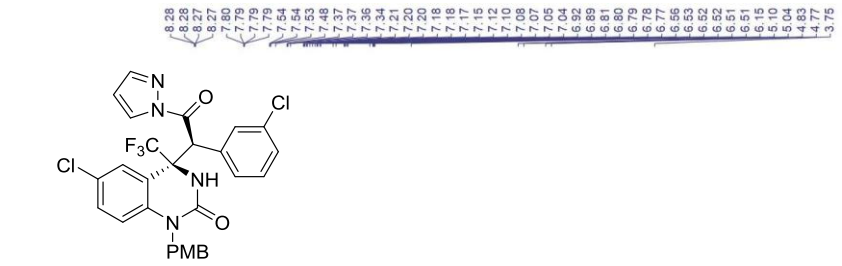


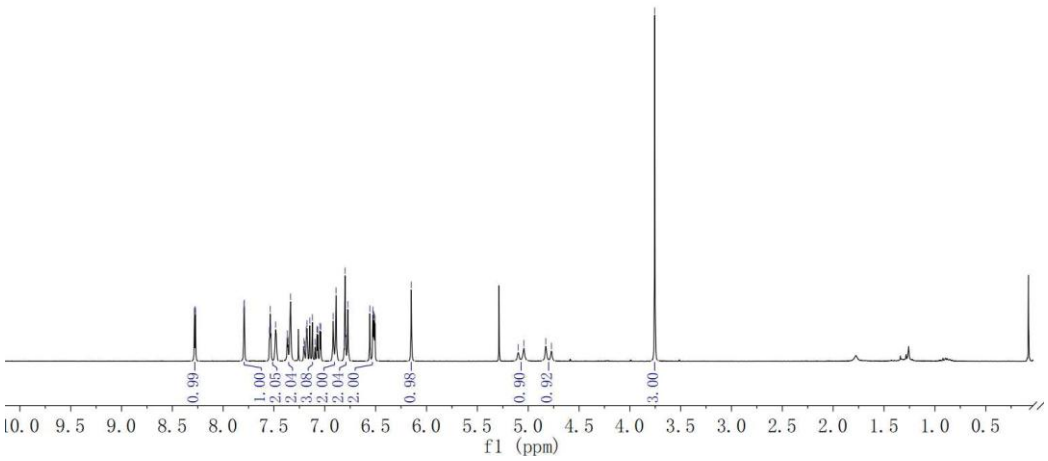
1 Det.A Ch1 / 254nm

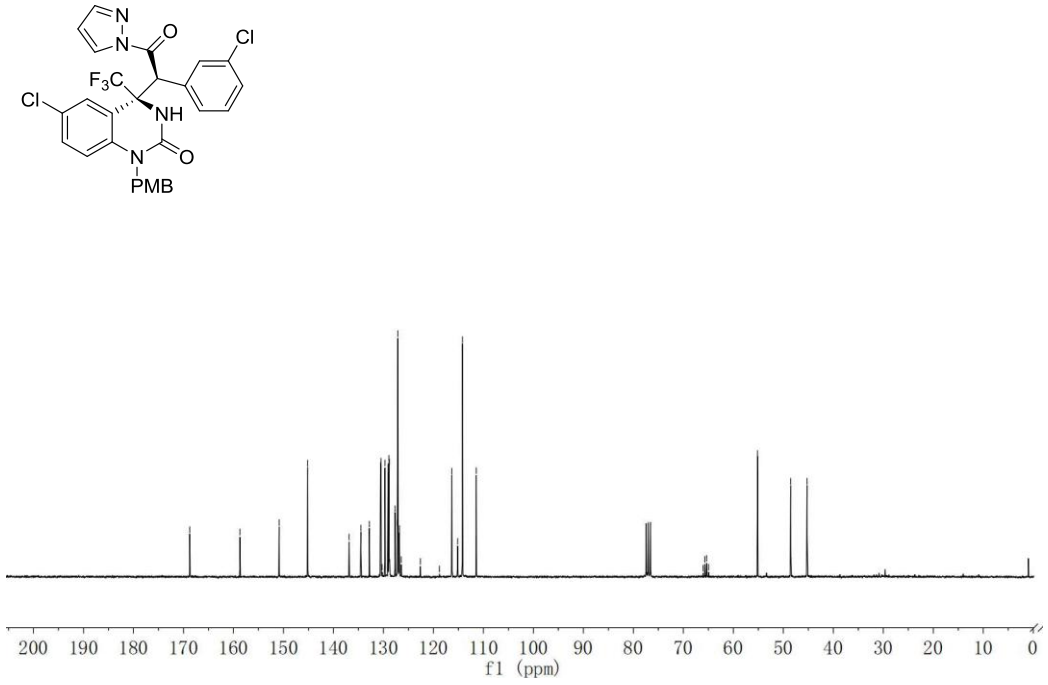
Detector A Ch1 254nm

Peak#	Ret. Time	Area	Height	Area %	Height %
1	7.506	22303	1567	2.438	2.355
2	8.396	892639	64989	97.562	97.645
Total		914942	66556	100.000	100.000

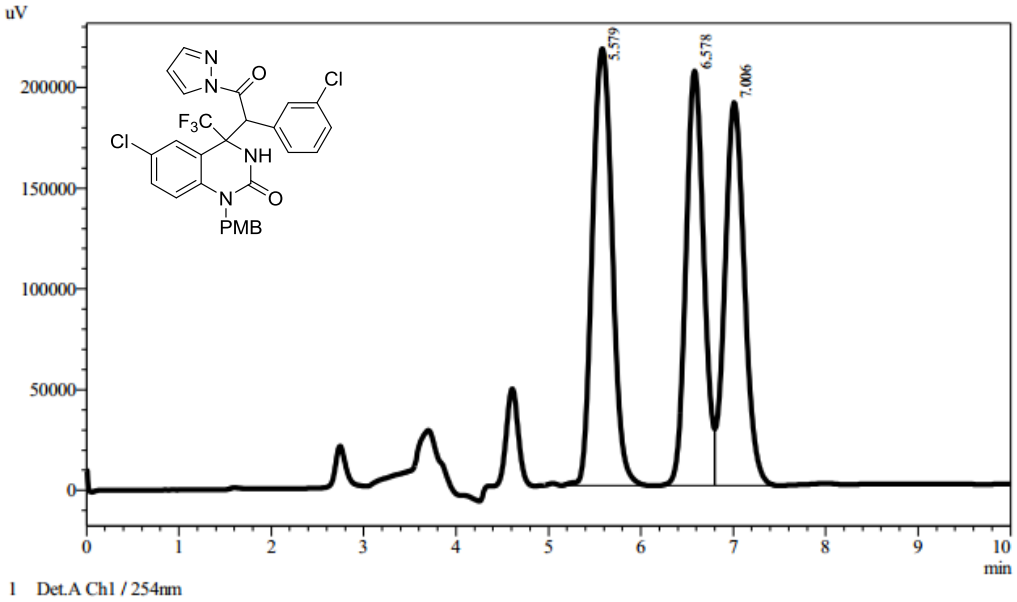
^{1}H and ^{13}C NMR of **3f**







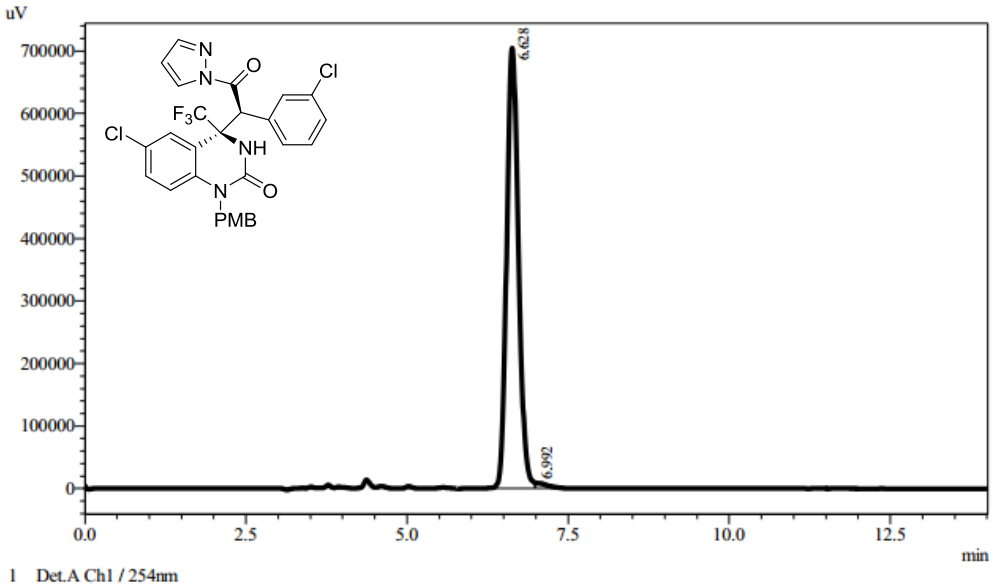
HPLC of **3f**



1 Det.A Ch1 / 254nm

Detector A Ch1 254nm

Peak#	Ret. Time	Area	Height	Area %	Height %
1	5.579	3228004	216895	36.801	35.390
2	6.578	2752707	205870	31.383	33.591
3	7.006	2790733	190099	31.816	31.018
Total		8771443	612864	100.000	100.000

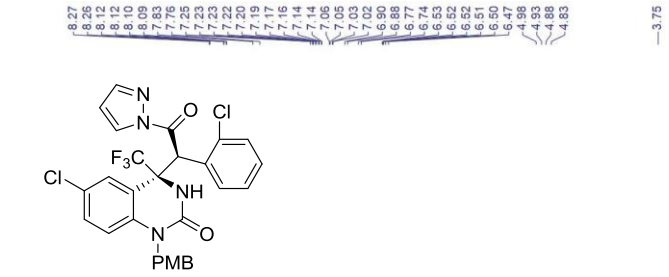


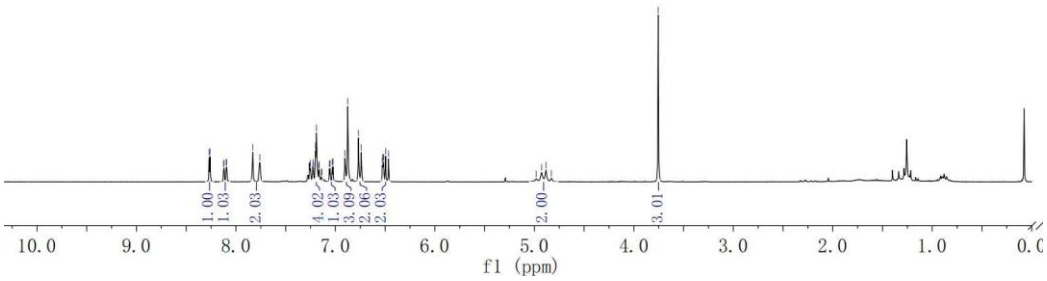
1 Det.A Ch1 / 254nm

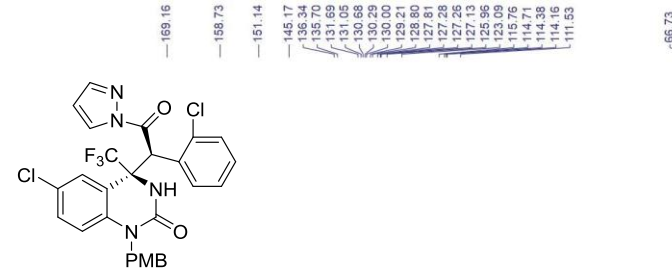
Detector A Ch1 254nm

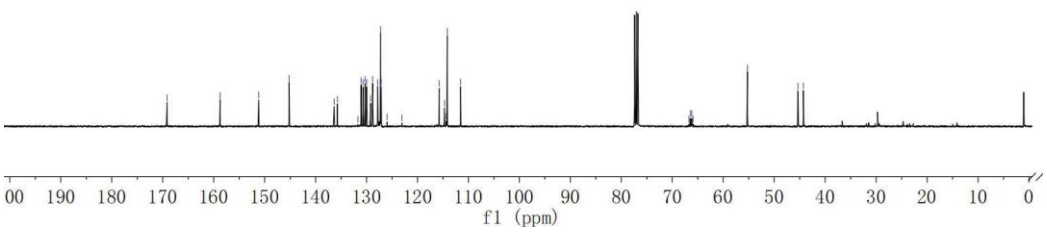
Peak#	Ret. Time	Area	Height	Area %	Height %
1	6.628	8954318	704081	98.791	98.799
2	6.992	109597	8559	1.209	1.201
Total		9063915	712639	100.000	100.000

^{1}H and ^{13}C NMR of **3g**

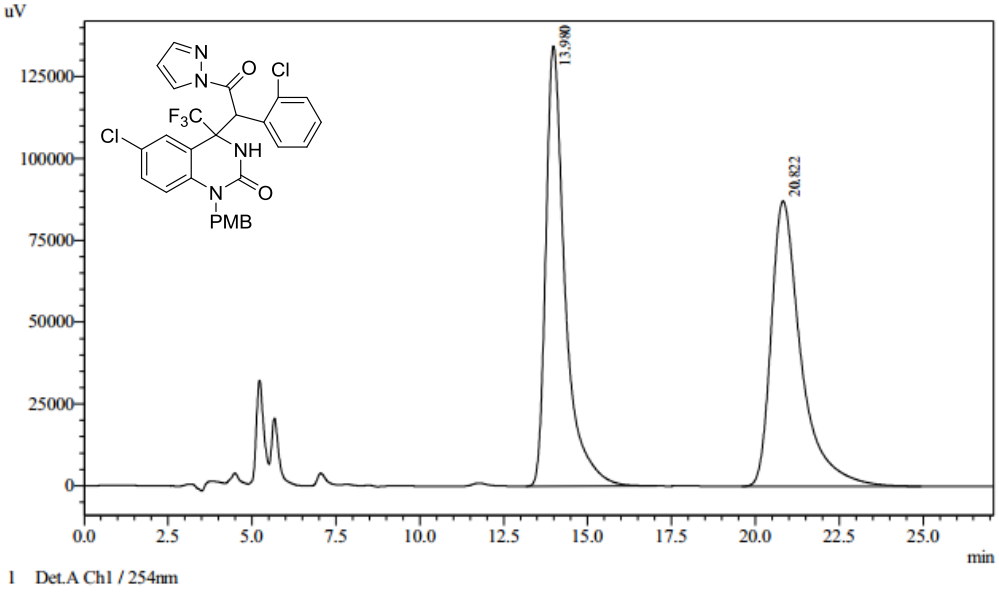






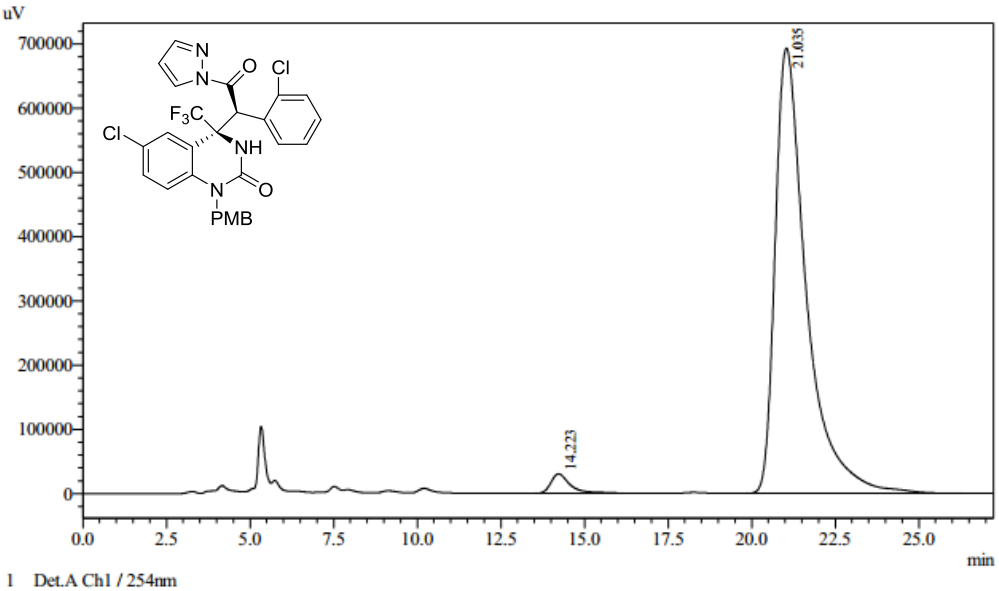


HPLC of **3g**



Detector A Ch1 254nm

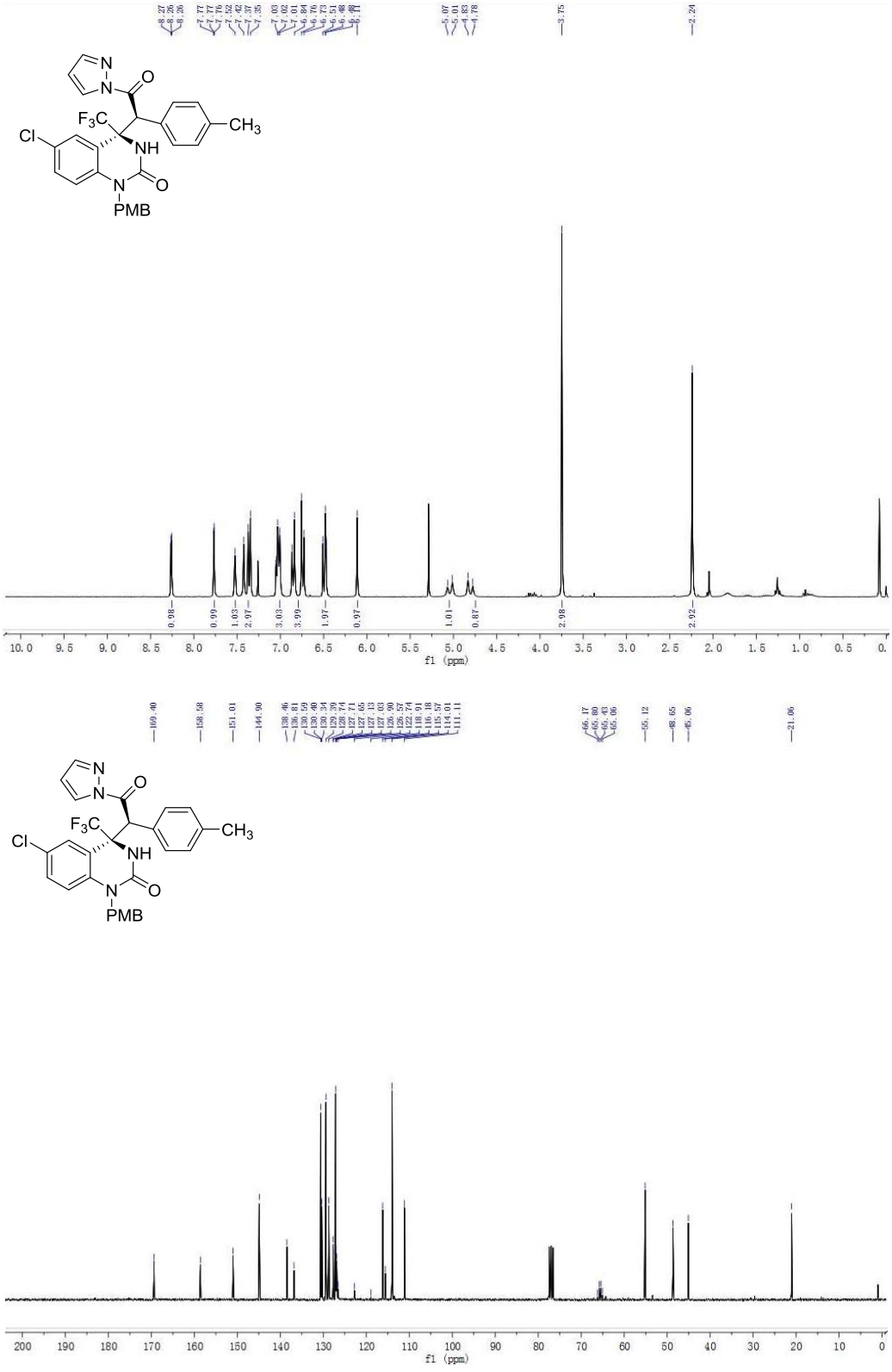
Peak#	Ret. Time	Area	Height	Area %	Height %
1	13.980	5374813	134507	49.947	60.663
2	20.822	5386154	87221	50.053	39.337
Total		10760967	221728	100.000	100.000



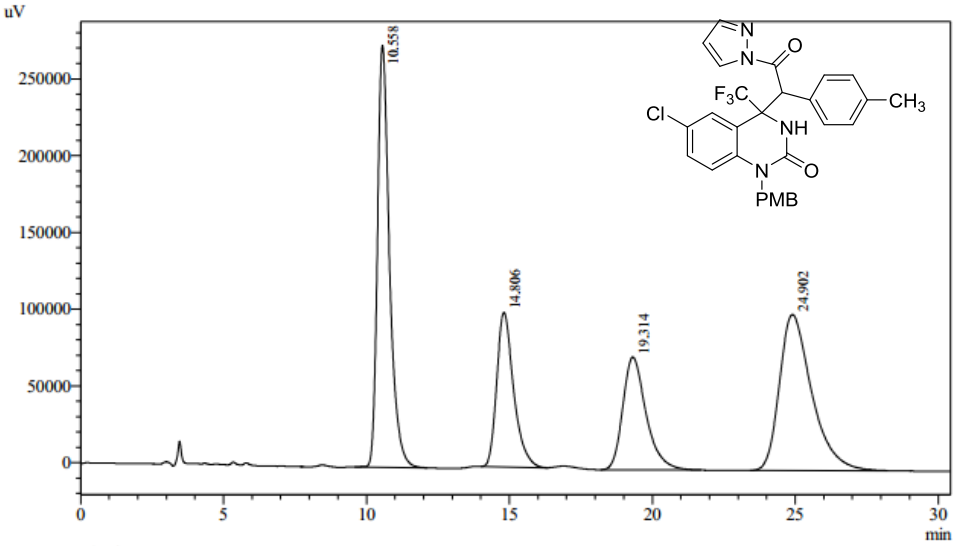
Detector A Ch1 254nm

Peak#	Ret. Time	Area	Height	Area %	Height %
1	14.223	1188398	30027	2.578	4.154
2	21.035	44910440	692885	97.422	95.846
Total		46098838	722912	100.000	100.000

^{1}H and ^{13}C NMR of **3h**



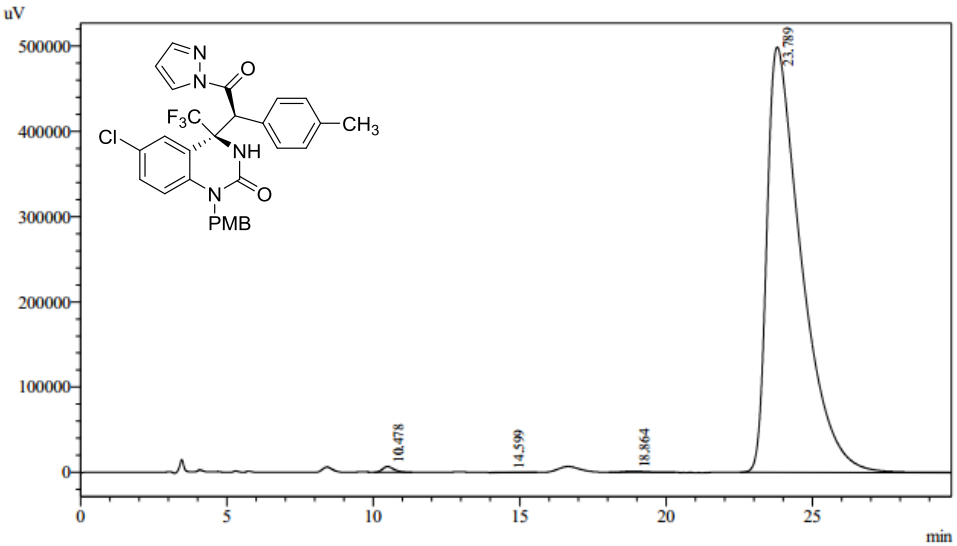
HPLC of **3h**



1 Det.A Ch1 / 254nm

Detector A Ch1 254nm

Peak#	Ret. Time	Area	Height	Area %	Height %
1	10.558	8028923	274729	32.999	49.918
2	14.806	4136222	100633	17.000	18.285
3	19.314	4177397	73457	17.169	13.347
4	24.902	7988298	101538	32.832	18.449
Total		24330840	550358	100.000	100.000

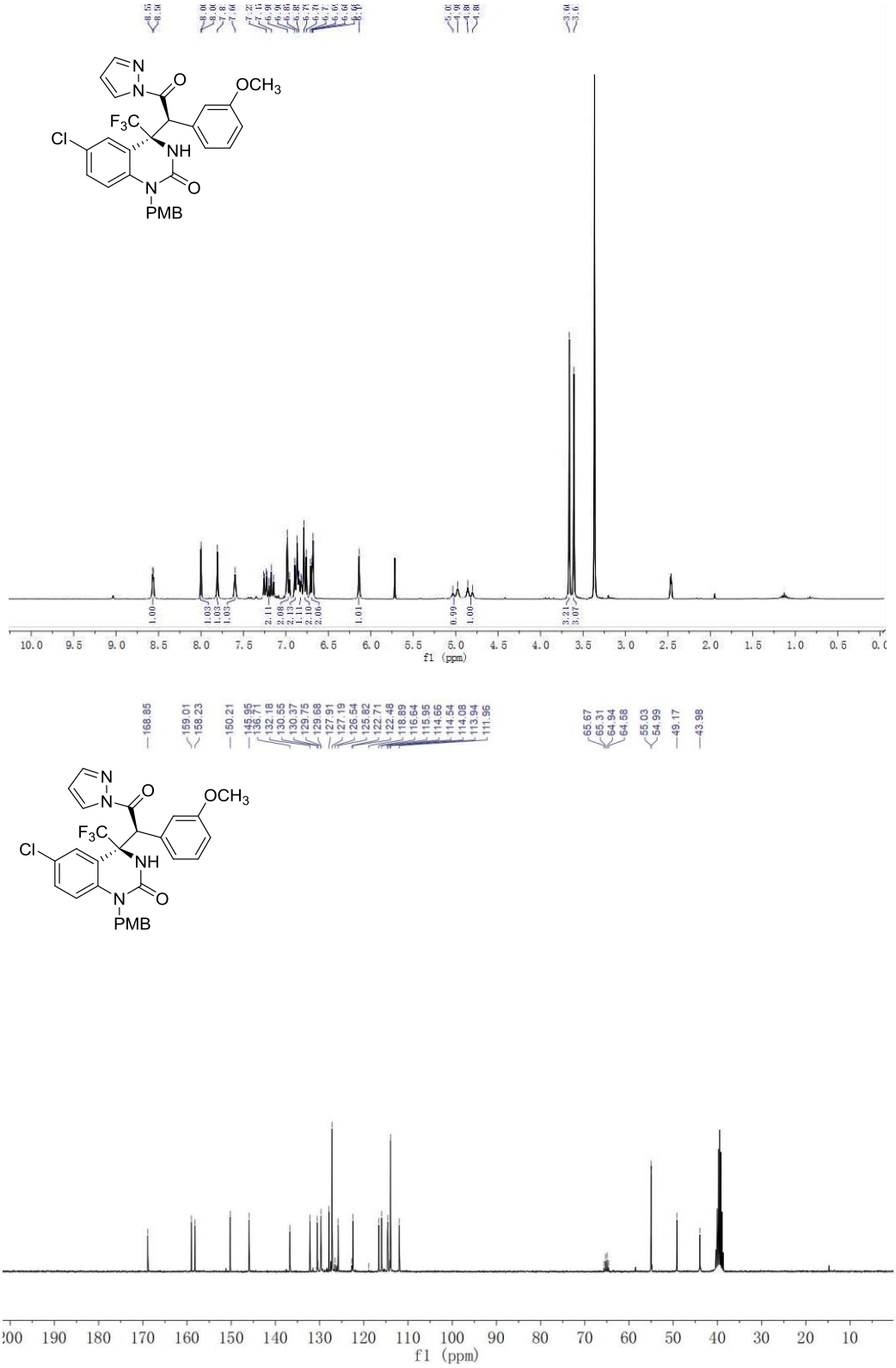


1 Det.A Ch1 / 254nm

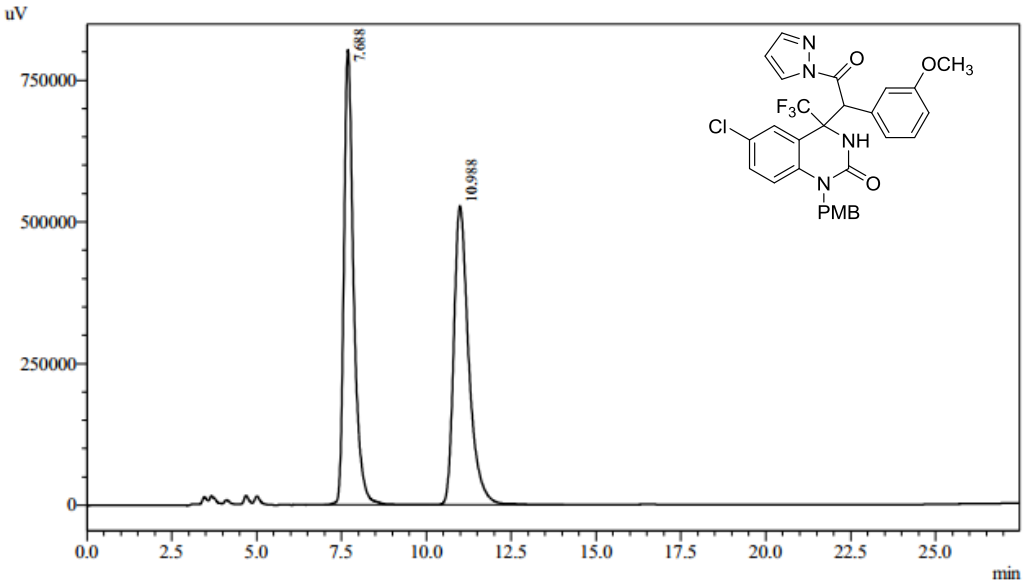
Detector A Ch1 254nm

Peak#	Ret. Time	Area	Height	Area %	Height %
1	10.478	184314	6701	0.449	1.321
2	14.599	13219	324	0.032	0.064
3	18.864	74770	1492	0.182	0.294
4	23.789	40741135	498590	99.336	98.320
Total		41013439	507107	100.000	100.000

^{1}H and ^{13}C NMR of **3i**



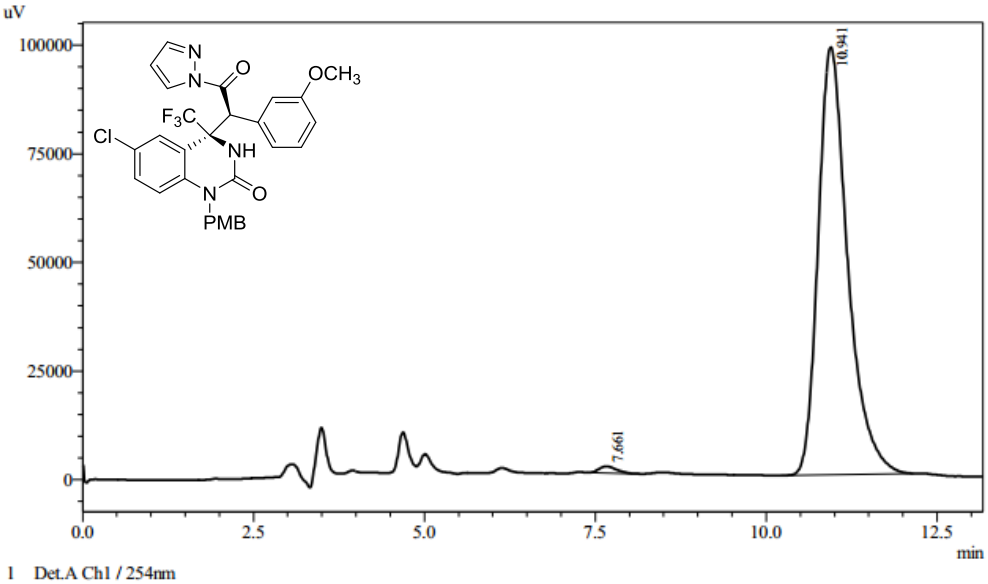
HPLC of **3i**



1 Det.A Ch1 / 254nm

Detector A Ch1 254nm

Peak#	Ret. Time	Area	Height	Area %	Height %
1	7.688	16097239	803211	49.923	60.348
2	10.988	16146932	527753	50.077	39.652
Total		32244171	1330964	100.000	100.000

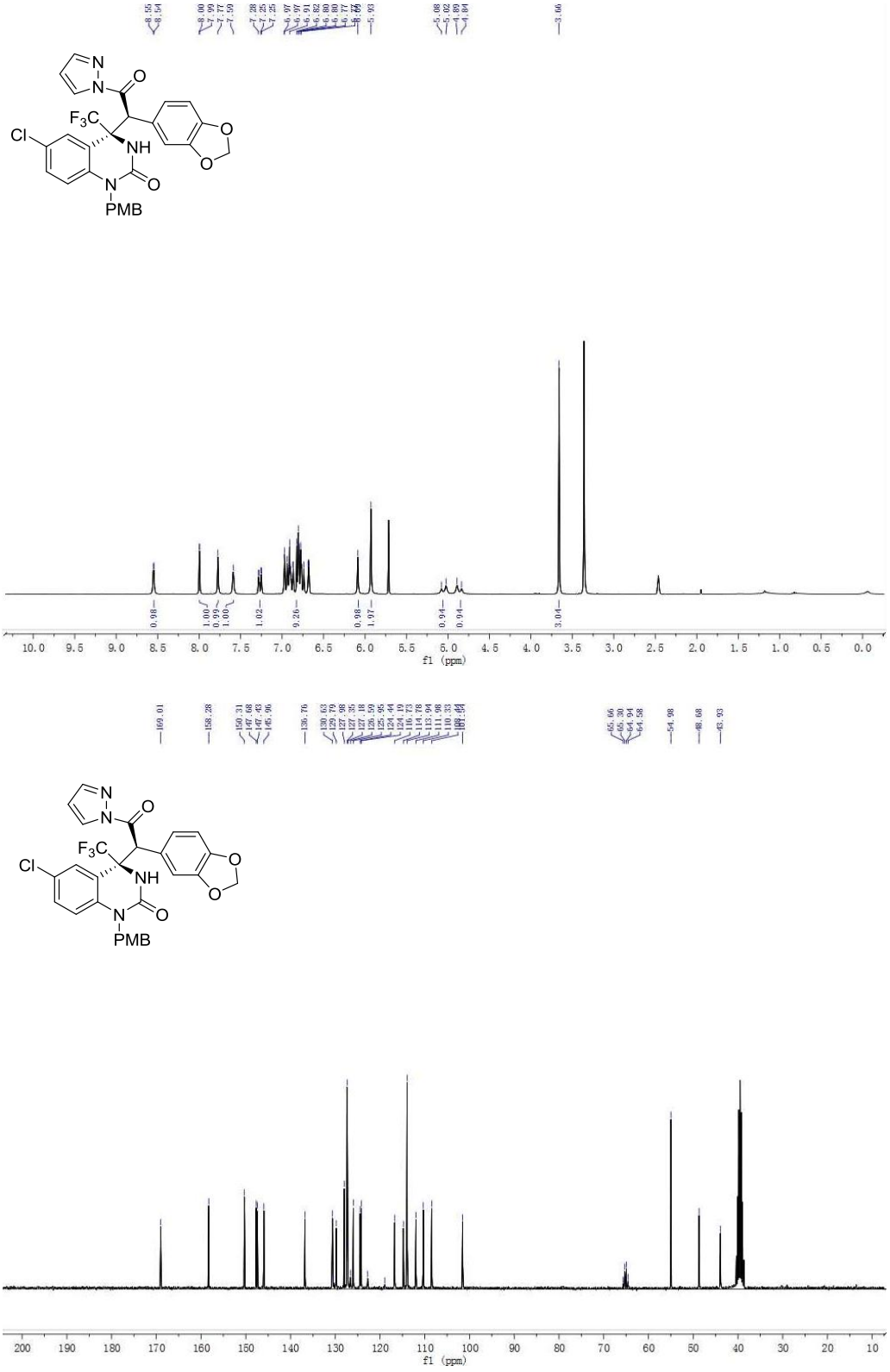


1 Det.A Ch1 / 254nm

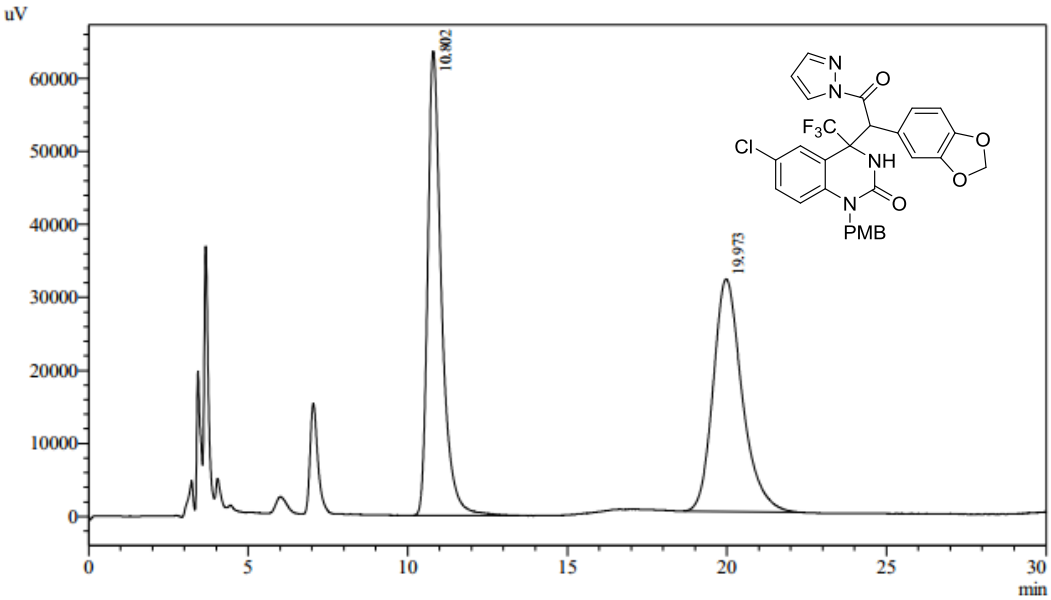
Detector A Ch1 254nm

Peak#	Ret. Time	Area	Height	Area %	Height %
1	7.661	27981	1557	0.936	1.558
2	10.941	2962456	98403	99.064	98.442
Total		2990437	99961	100.000	100.000

^{1}H and ^{13}C NMR of **3j**



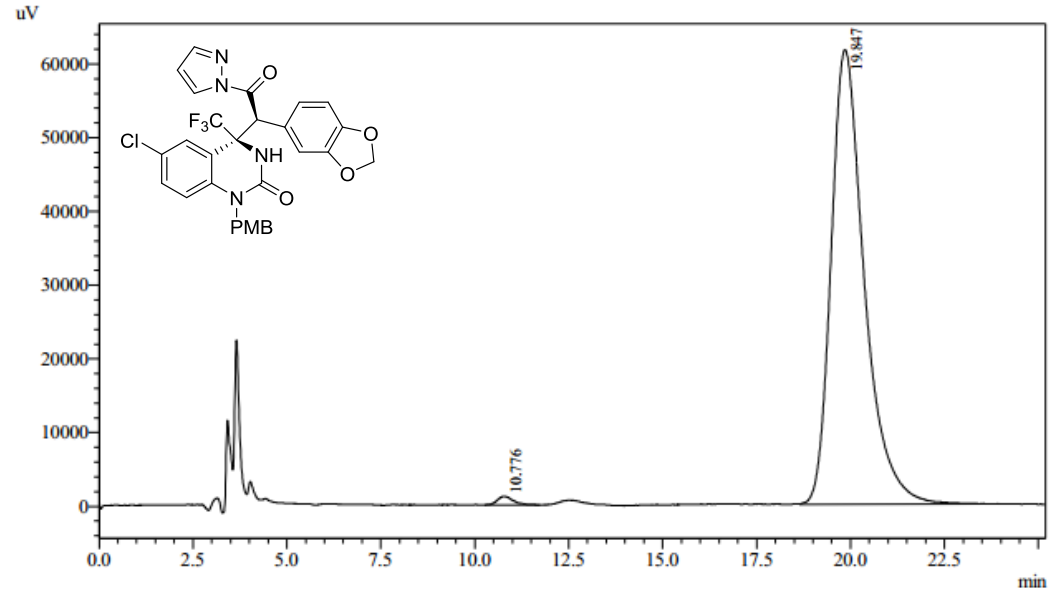
HPLC of **3j**



1 Det.A Ch1 / 254nm

Detector A Ch1 254nm

Peak#	Ret. Time	Area	Height	Area %	Height %
1	10.802	1929522	63611	48.975	66.639
2	19.973	2010274	31845	51.025	33.361
Total		3939796	95455	100.000	100.000

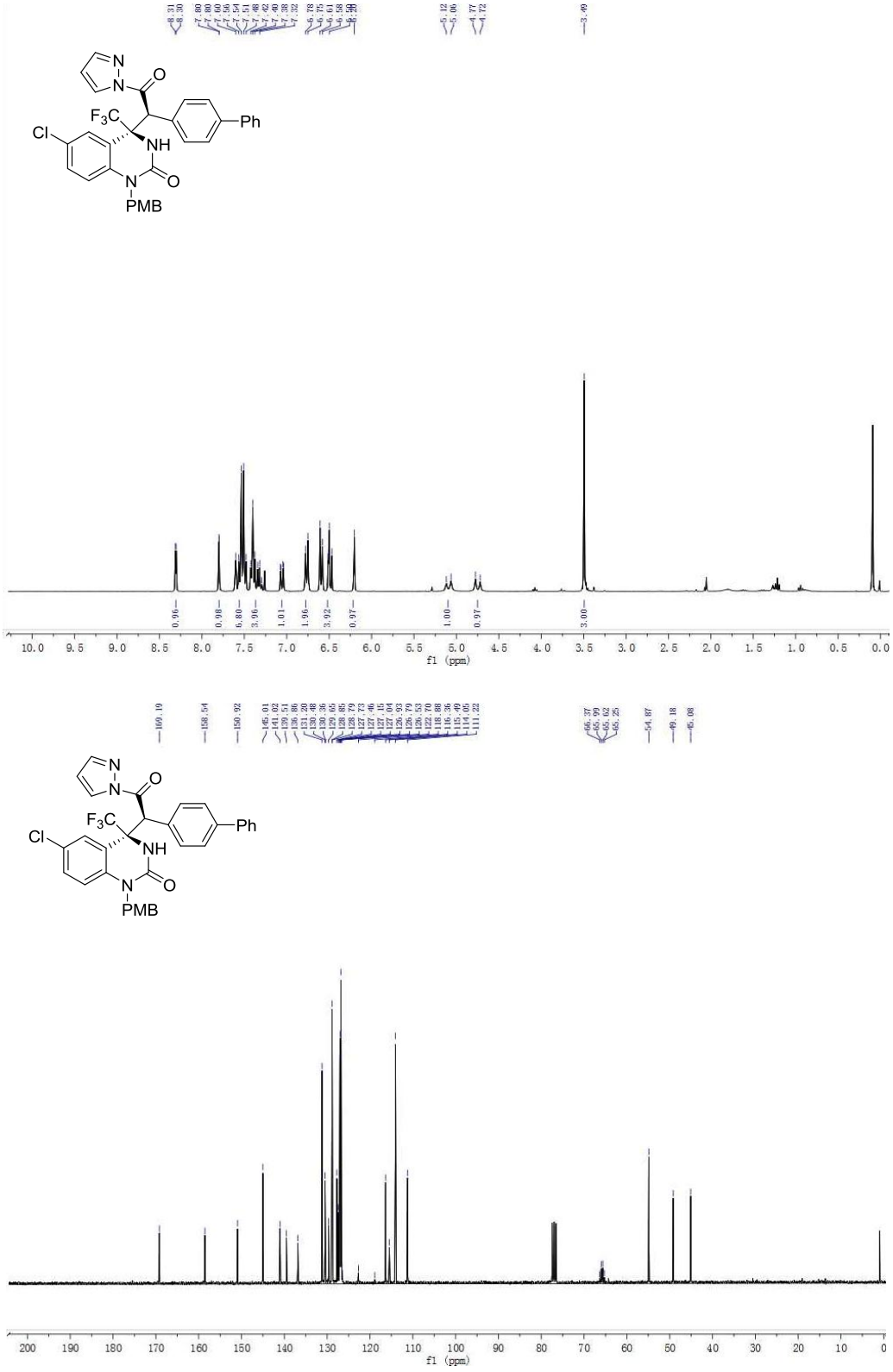


1 Det.A Ch1 / 254nm

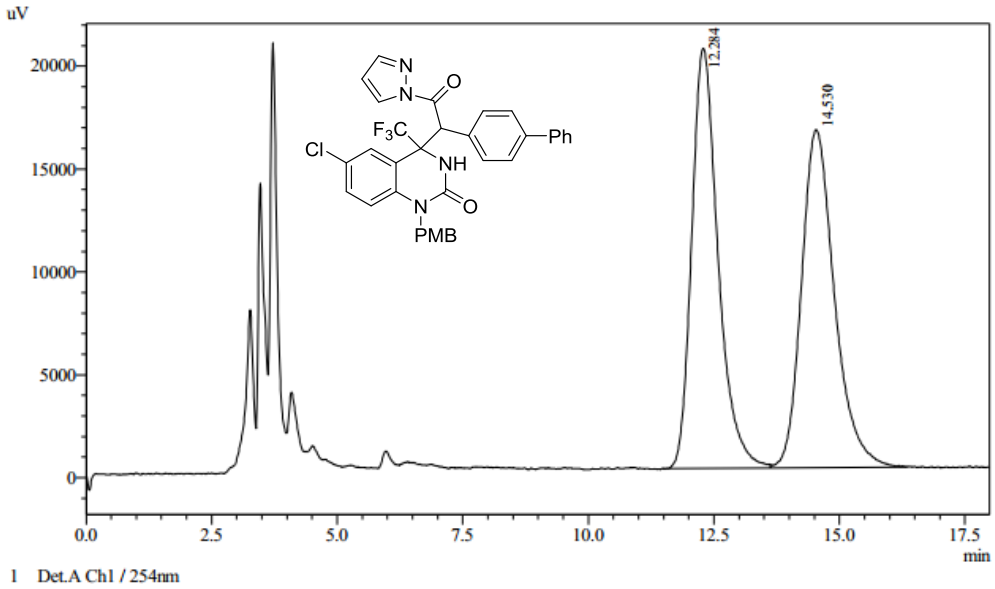
Detector A Ch1 254nm

Peak#	Ret. Time	Area	Height	Area %	Height %
1	10.776	34668	1165	0.906	1.855
2	19.847	3789860	61645	99.094	98.145
Total		3824528	62810	100.000	100.000

^{1}H and ^{13}C NMR of **3k**



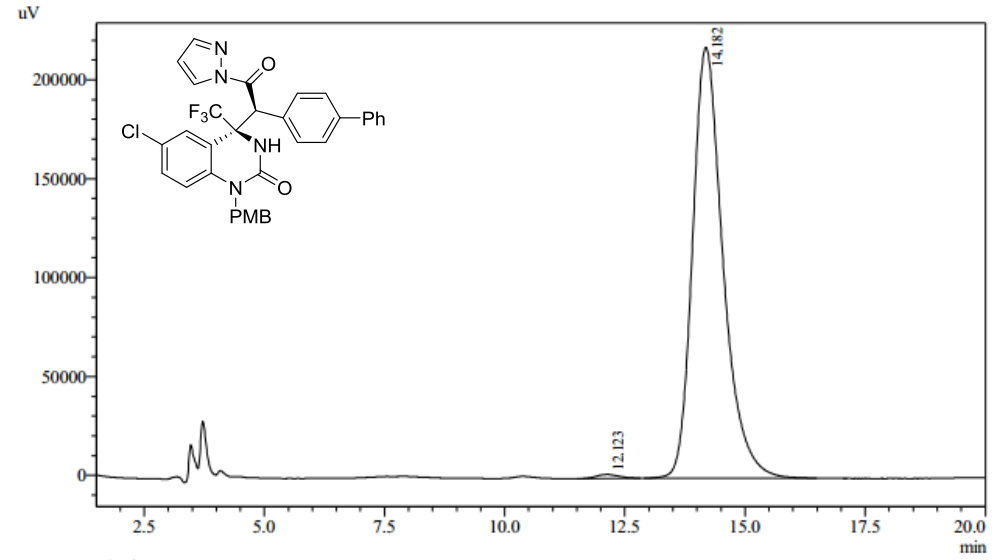
HPLC of **3k**



1 Det.A Ch1 / 254nm

Detector A Ch1 254nm

Peak#	Ret. Time	Area	Height	Area %	Height %
1	12.284	747162	20417	49.905	55.417
2	14.530	750013	16426	50.095	44.583
Total		1497175	36843	100.000	100.000

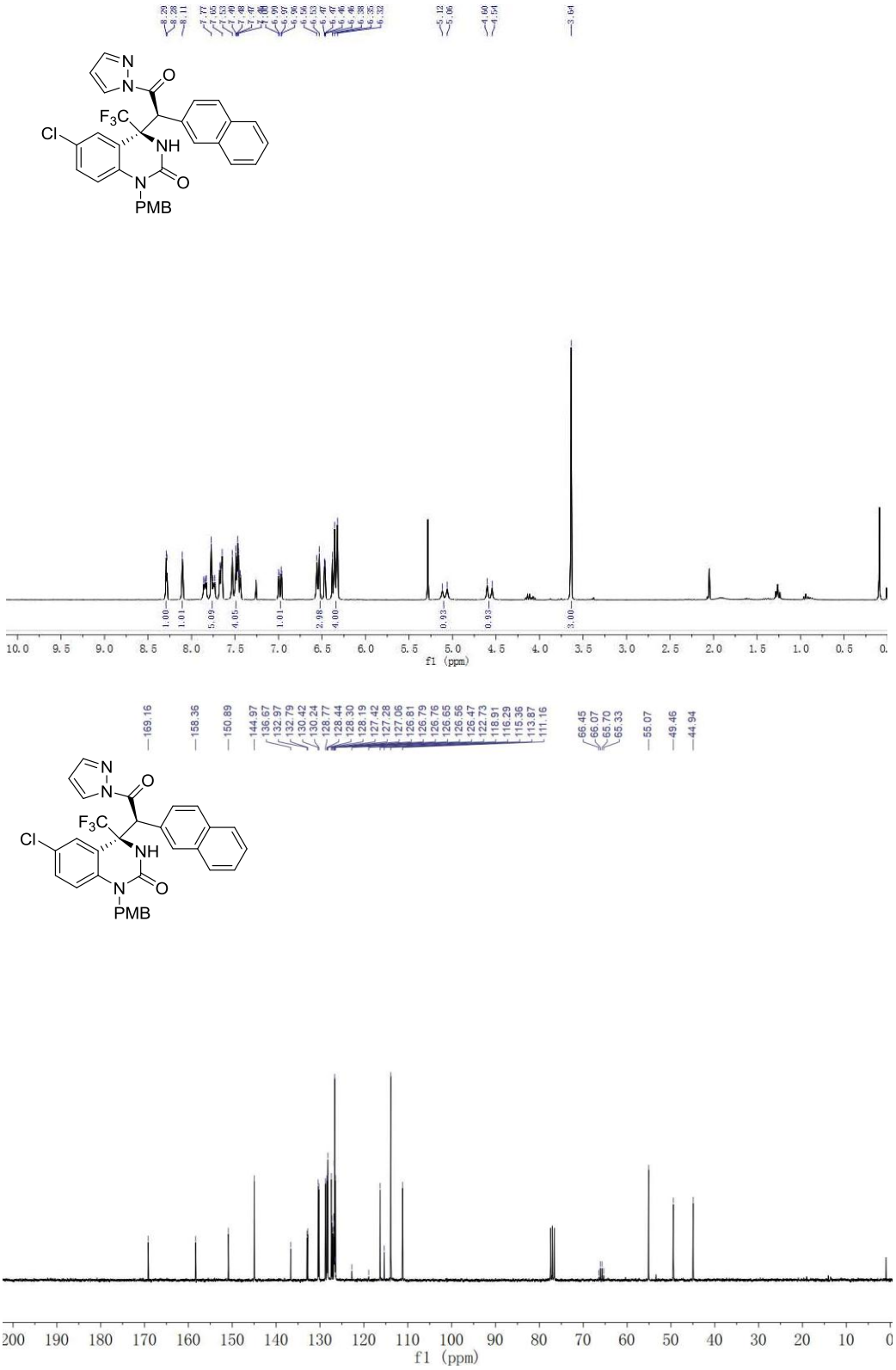


1 Det.A Ch1 / 254nm

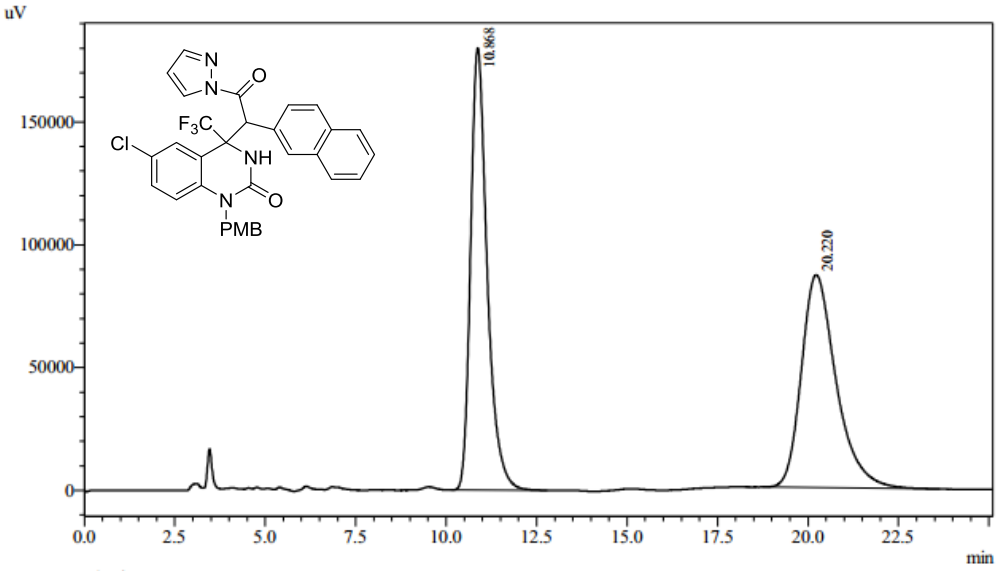
Detector A Ch1 254nm

Peak#	Ret. Time	Area	Height	Area %	Height %
1	12.123	66039	2033	0.682	0.925
2	14.182	9623253	217744	99.318	99.075
Total		9689293	219777	100.000	100.000

^{1}H and ^{13}C NMR of **3l**



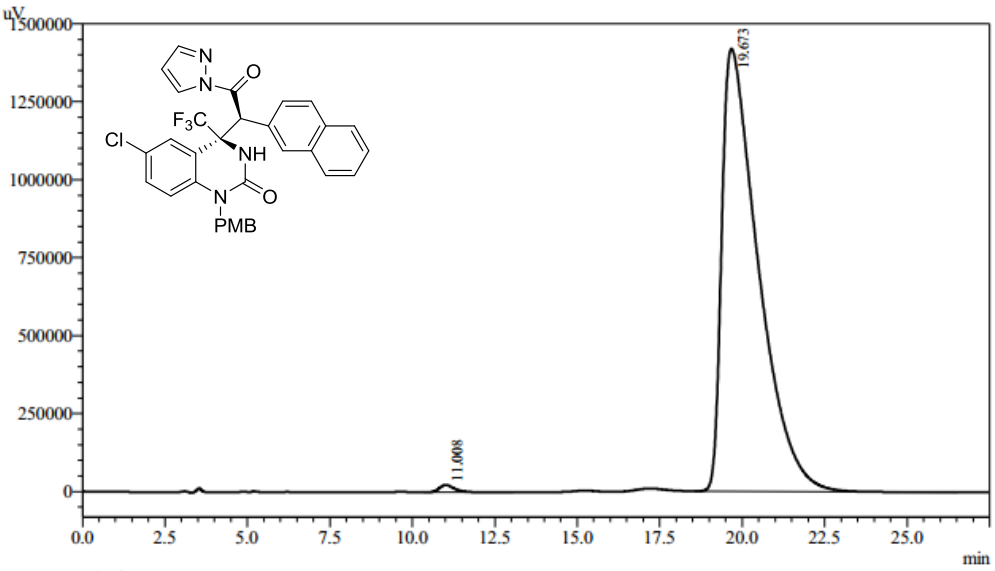
HPLC of **3l**



1 Det.A Ch1 / 254nm

Detector A Ch1 254nm

Peak#	Ret. Time	Area	Height	Area %	Height %
1	10.868	5760400	180043	49.770	67.516
2	20.220	5813546	86624	50.230	32.484
Total		11573946	266667	100.000	100.000

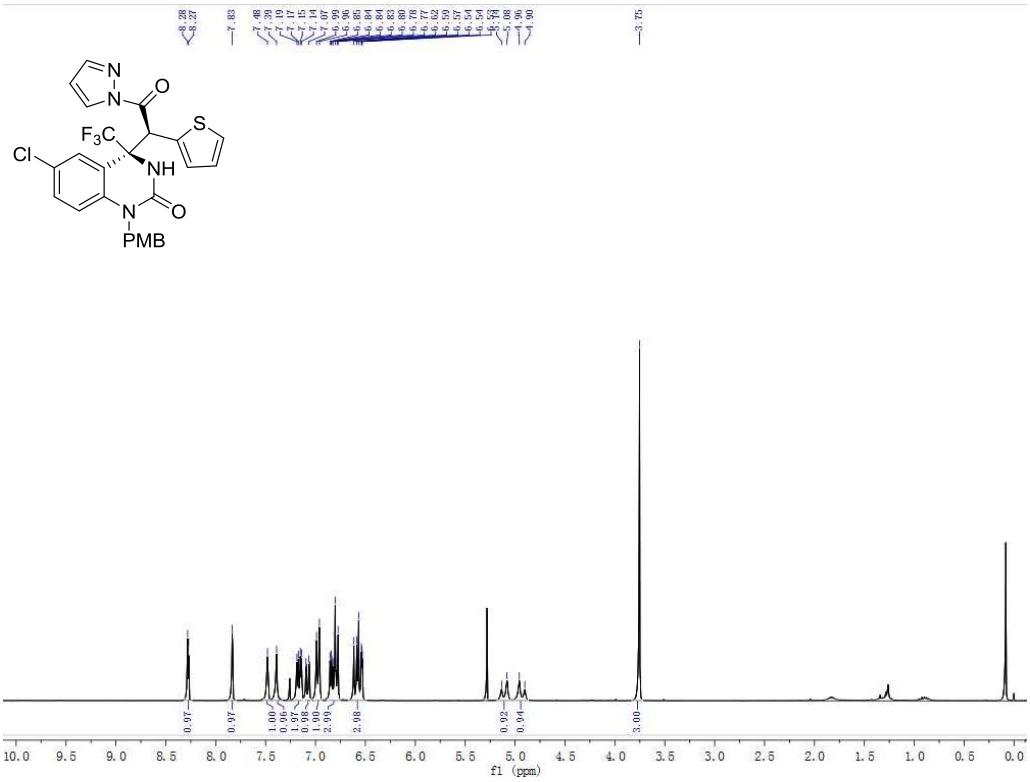


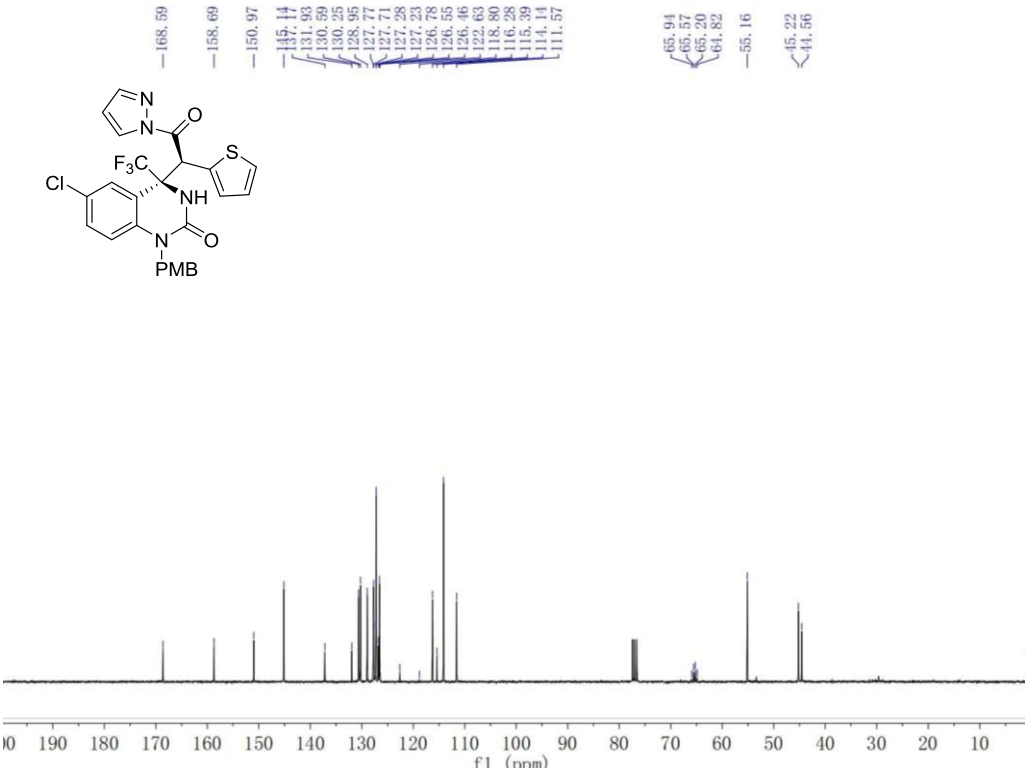
1 Det.A Ch1 / 254nm

Detector A Ch1 254nm

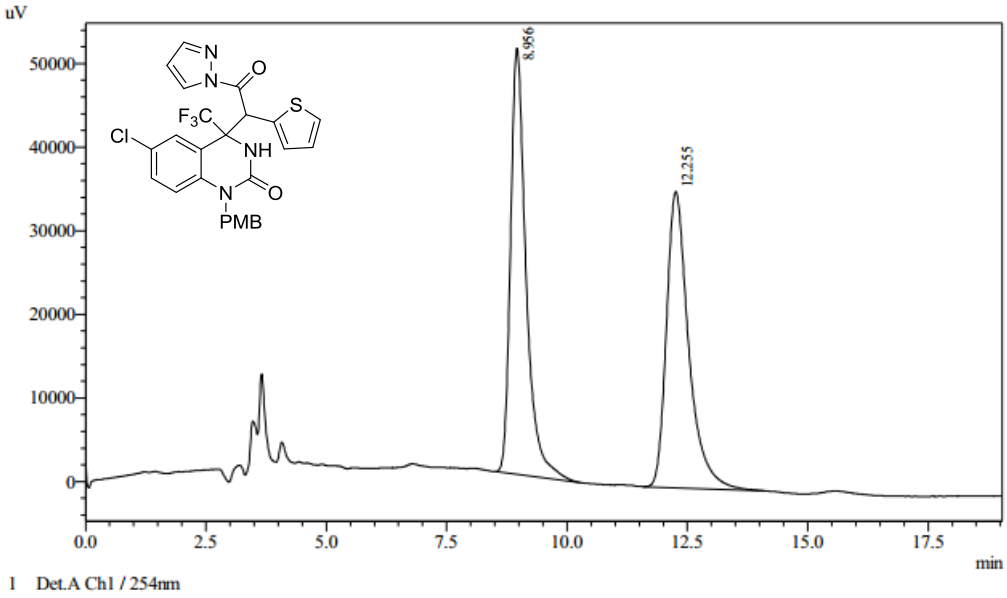
Peak#	Ret. Time	Area	Height	Area %	Height %
1	11.008	751832	23360	0.685	1.620
2	19.673	109065696	1418869	99.315	98.380
Total		109817528	1442229	100.000	100.000

^{1}H and ^{13}C NMR of **3m**





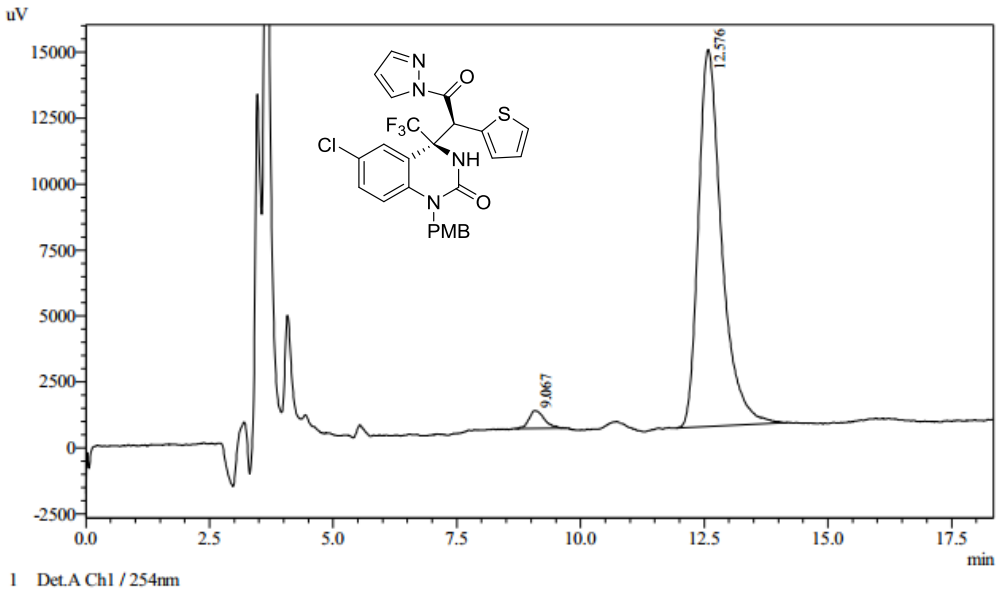
HPLC of **3m**



1 Det.A Ch1 / 254nm

Detector A Ch1 254nm

Peak#	Ret. Time	Area	Height	Area %	Height %
1	8.956	1145131	50963	50.142	58.978
2	12.255	1138663	35446	49.858	41.022
Total		2283793	86409	100.000	100.000

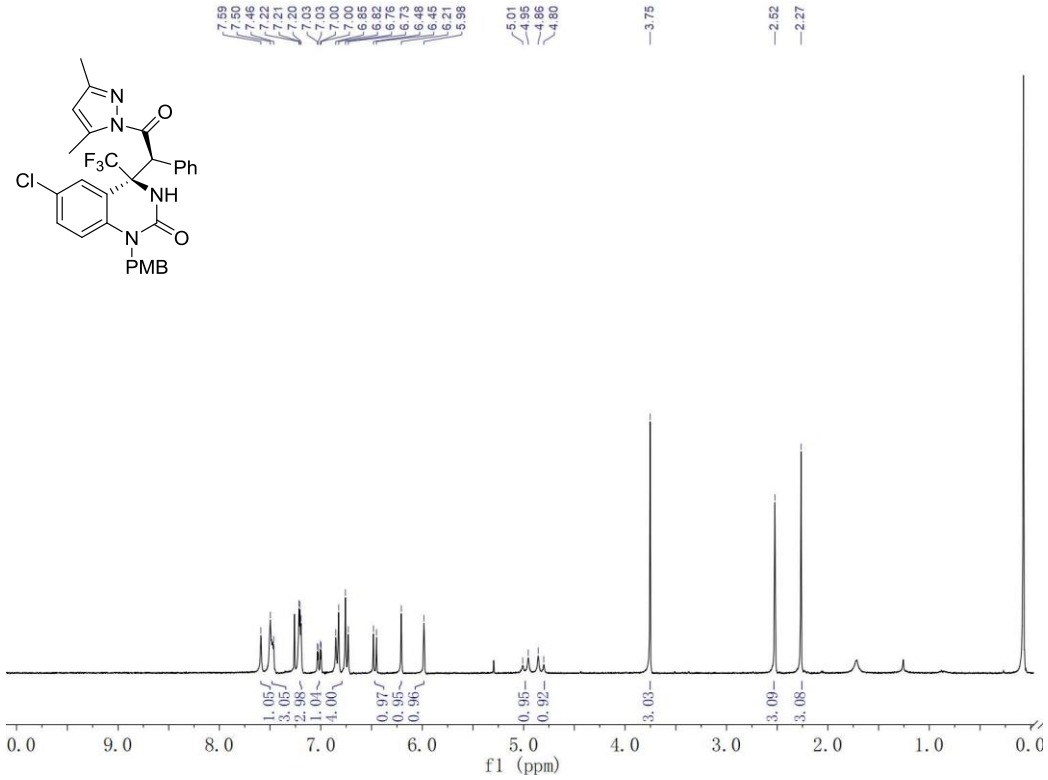


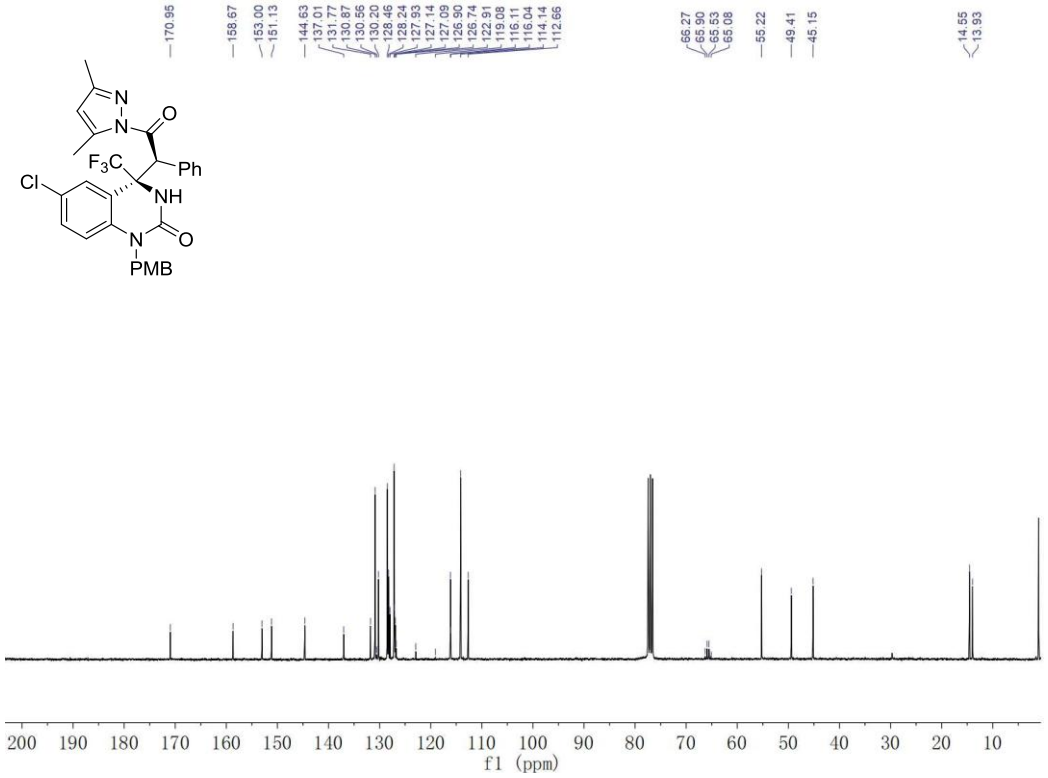
1 Det.A Ch1 / 254nm

Detector A Ch1 254nm

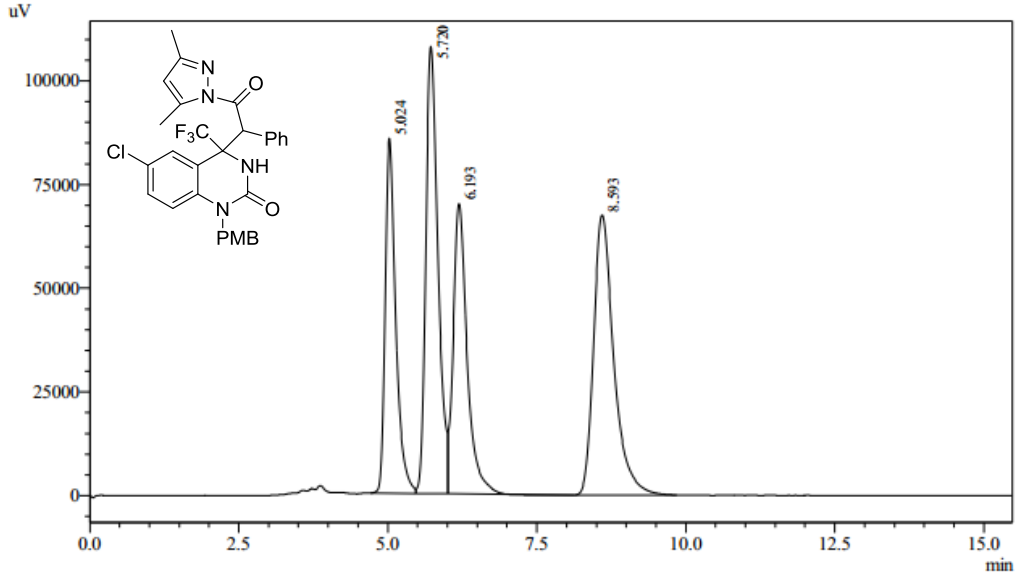
Peak#	Ret. Time	Area	Height	Area %	Height %
1	9.067	14352	672	2.962	4.492
2	12.576	470122	14292	97.038	95.508
Total		484474	14965	100.000	100.000

^{1}H and ^{13}C NMR of **3n**





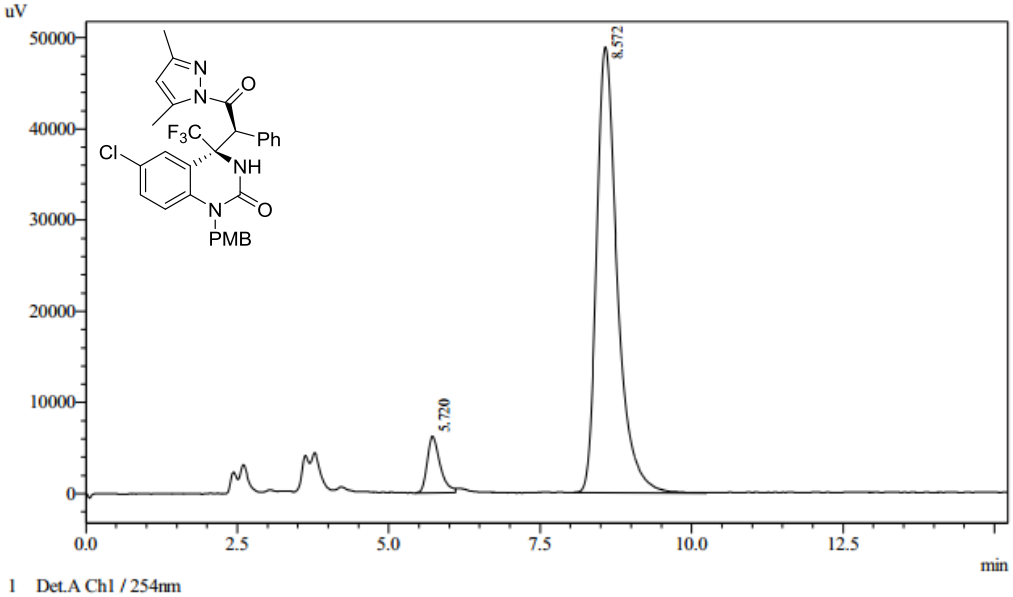
HPLC of **3n**



1 Det.A Ch1 / 254nm

Detector A Ch1 254nm

Peak#	Ret. Time	Area	Height	Area %	Height %
1	5.024	1059126	85589	19.938	25.864
2	5.720	1533790	107830	28.874	32.585
3	6.193	1130846	69981	21.288	21.147
4	8.593	1588308	67523	29.900	20.404
Total		5312069	330923	100.000	100.000

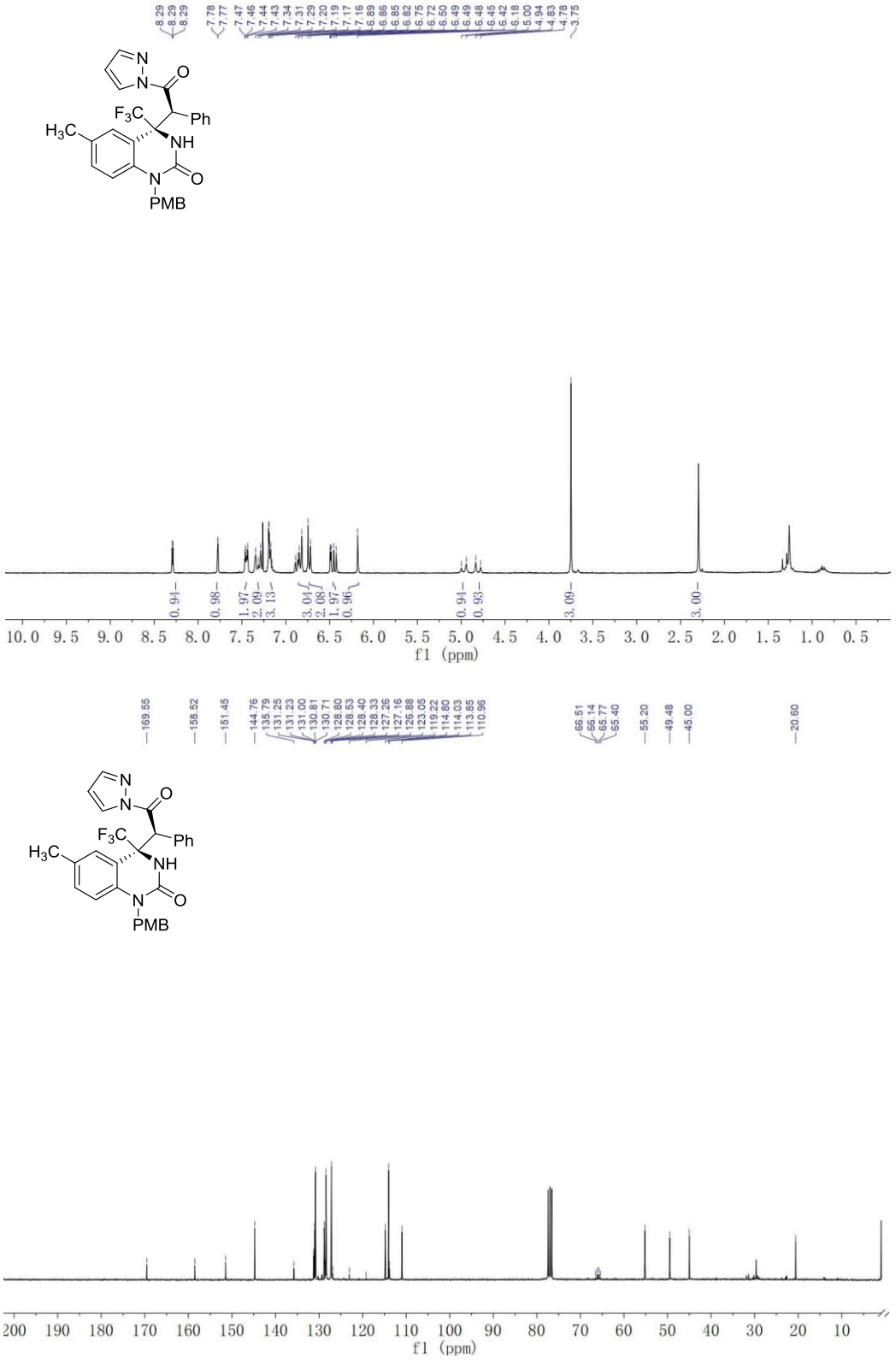


1 Det.A Ch1 / 254nm

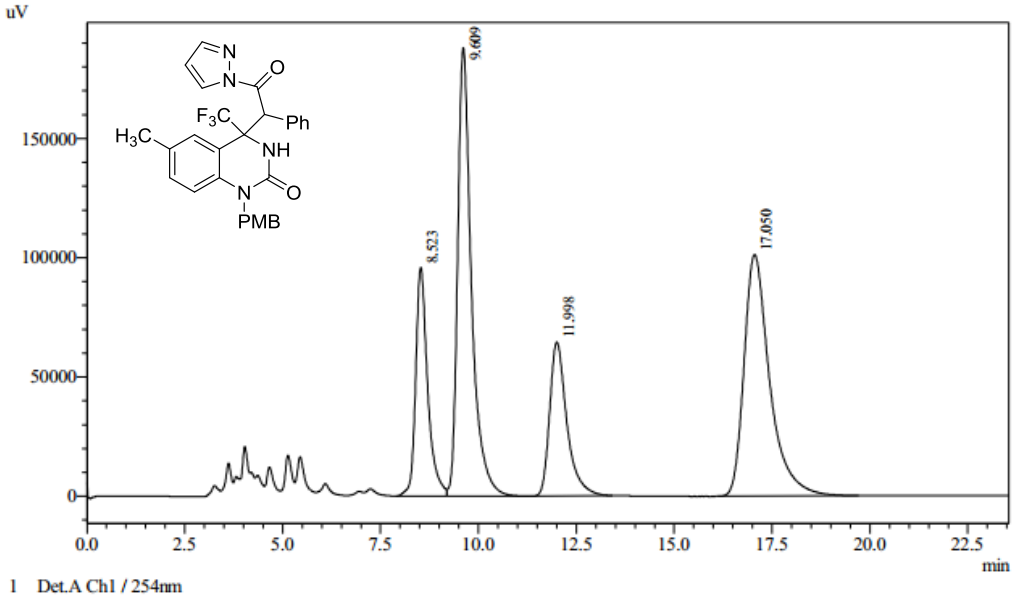
Detector A Ch1 254nm

Peak#	Ret. Time	Area	Height	Area %	Height %
1	5.720	93921	6213	7.506	11.277
2	8.572	1157367	48884	92.494	88.723
Total		1251288	55098	100.000	100.000

^{1}H and ^{13}C NMR of **3o**



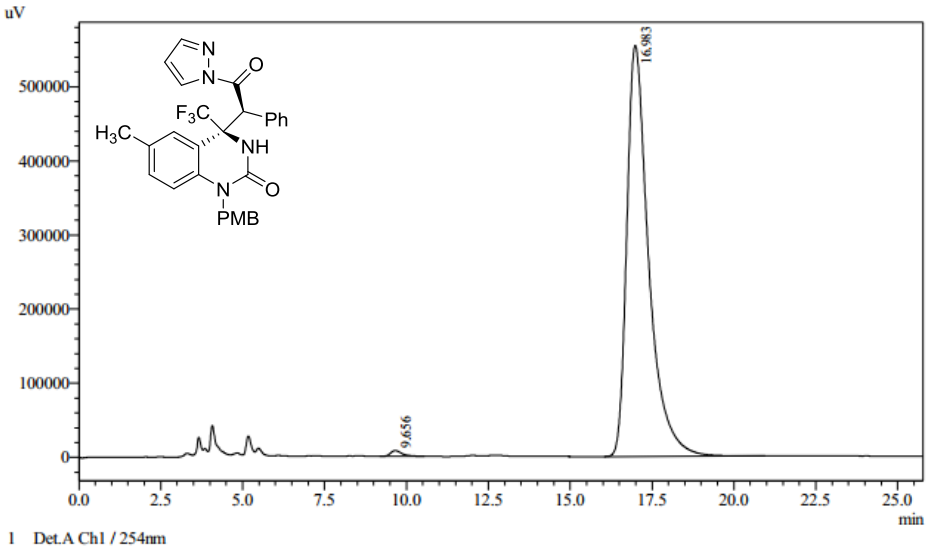
HPLC of **3o**



1 Det.A Ch1 / 254nm

Detector A Ch1 254nm

Peak#	Ret. Time	Area	Height	Area %	Height %
1	8.523	2044315	95952	15.413	21.332
2	9.609	4611897	188025	34.772	41.801
3	11.998	1986253	64608	14.976	14.363
4	17.050	4620766	101227	34.839	22.504
Total		13263231	449812	100.000	100.000

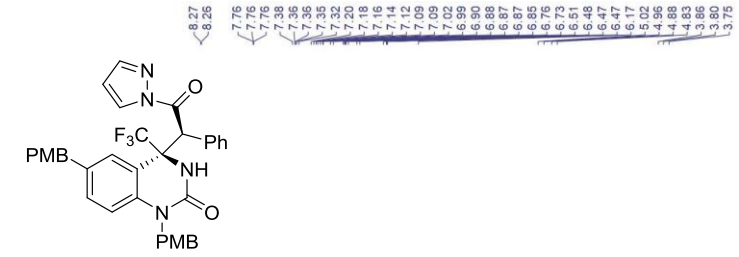


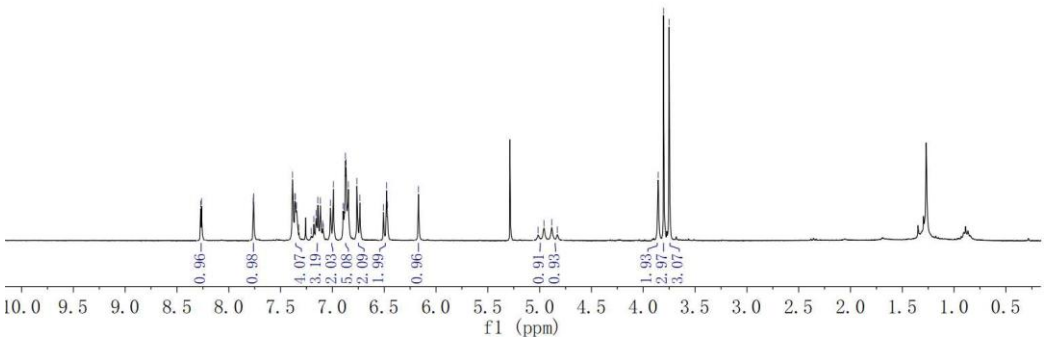
1 Det.A Ch1 / 254nm

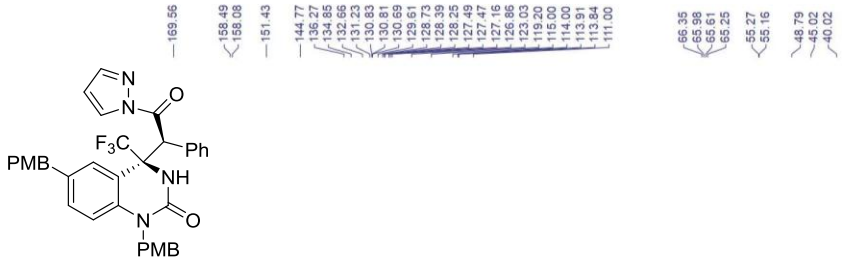
Detector A Ch1 254nm

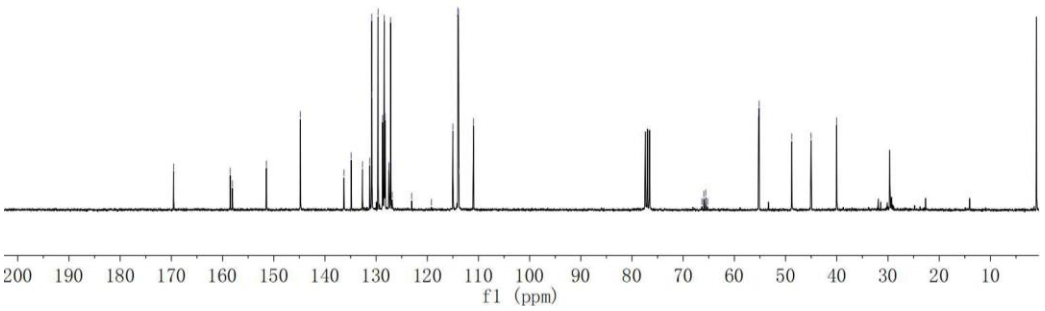
Peak#	Ret. Time	Area	Height	Area %	Height %
1	9.656	184691	7825	0.712	1.392
2	16.983	25739282	554528	99.288	98.608
Total		25923974	562354	100.000	100.000

^{1}H and ^{13}C NMR of **3p**

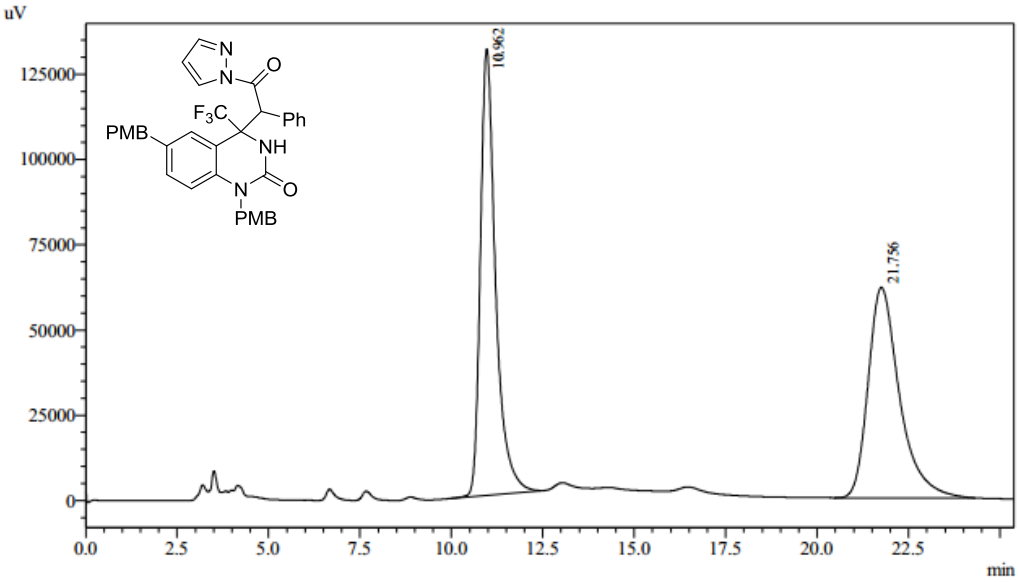








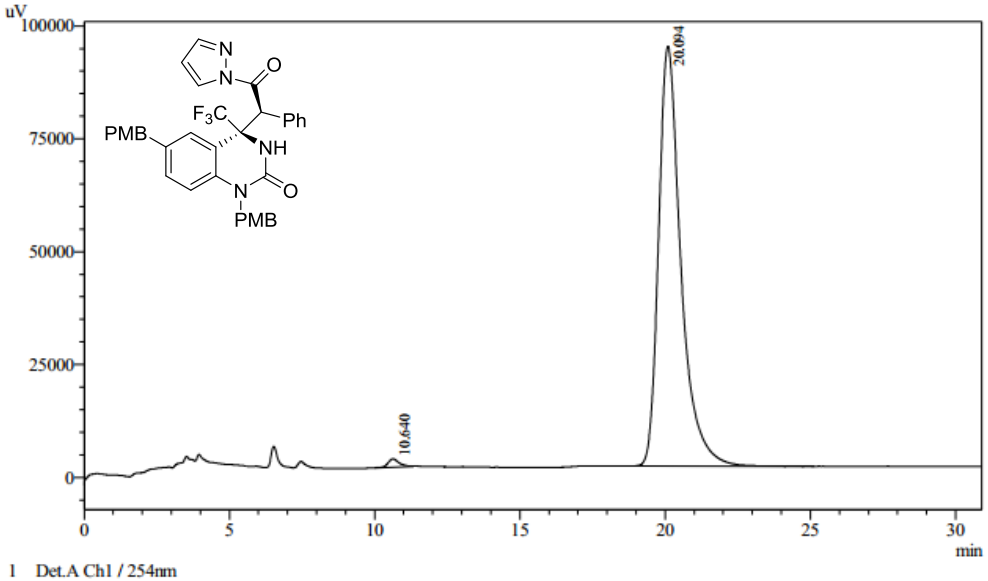
HPLC of **3p**



1 Det.A Ch1 / 254nm

Detector A Ch1 254nm

Peak#	Ret. Time	Area	Height	Area %	Height %
1	10.962	3791148	130966	50.682	67.964
2	21.756	3689090	61734	49.318	32.036
Total		7480238	192700	100.000	100.000

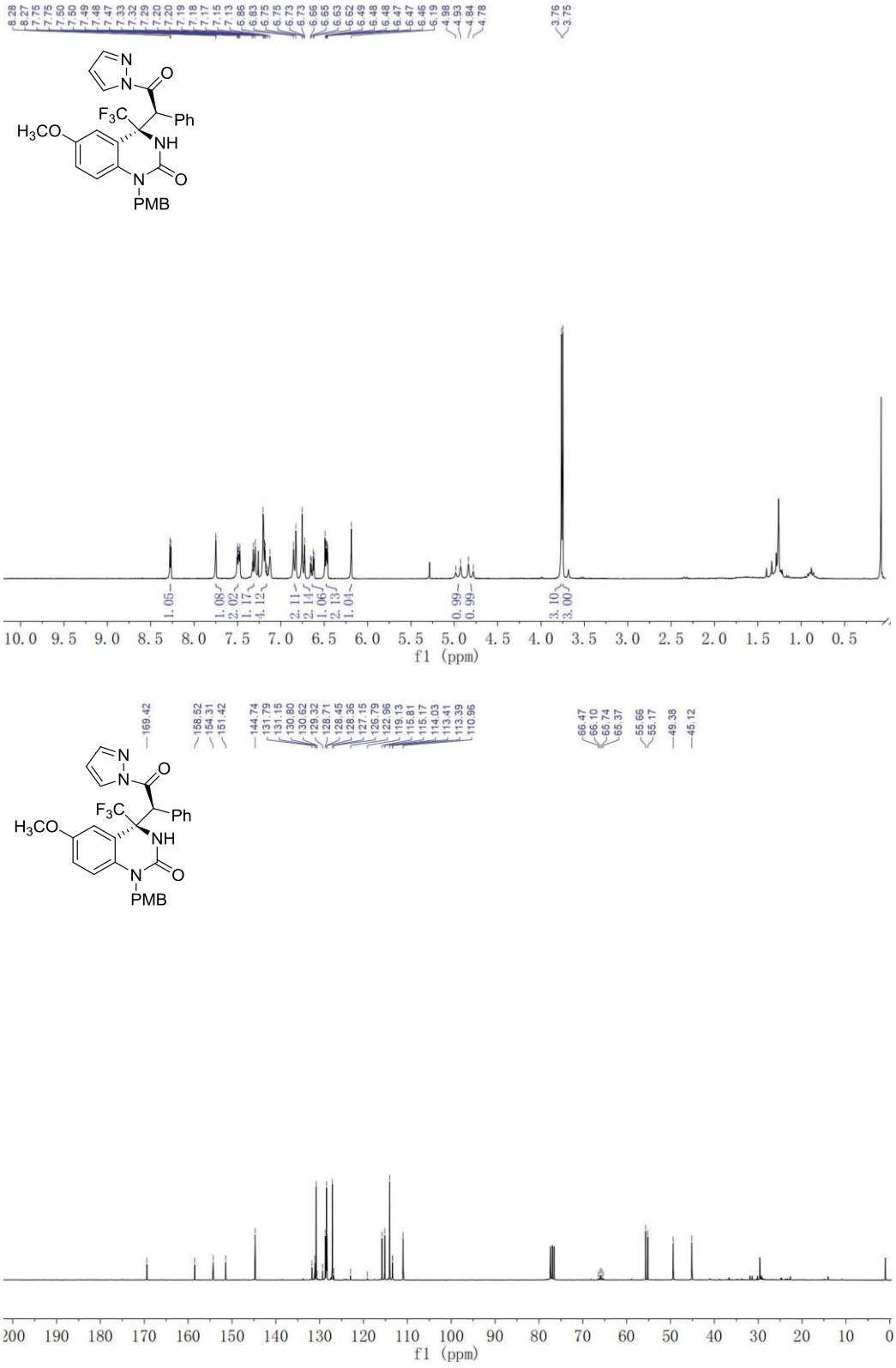


1 Det.A Ch1 / 254nm

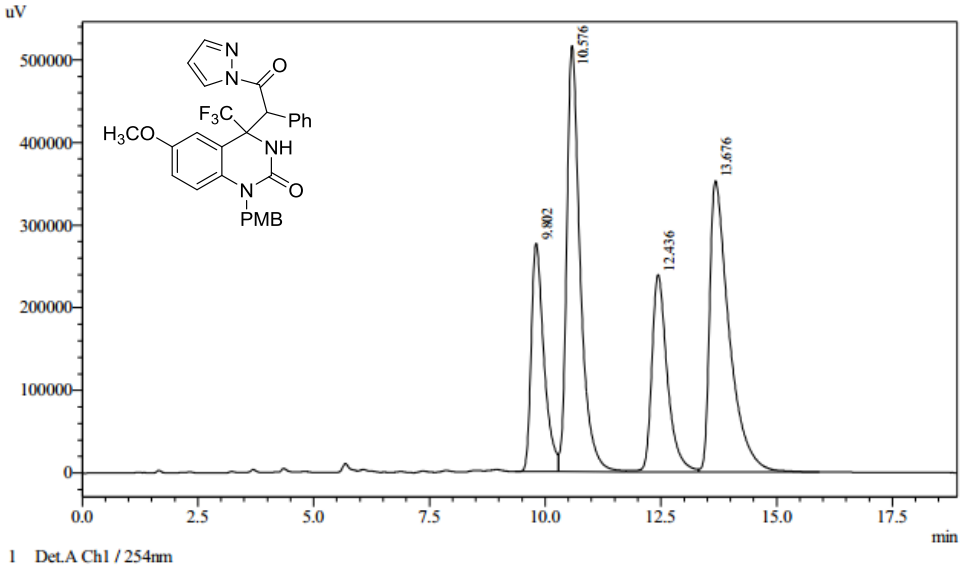
Detector A Ch1 254nm

Peak#	Ret. Time	Area	Height	Area %	Height %
1	10.640	46336	1773	0.924	1.871
2	20.094	4966817	92967	99.076	98.129
Total		5013154	94740	100.000	100.000

^{1}H and ^{13}C NMR of **3q**



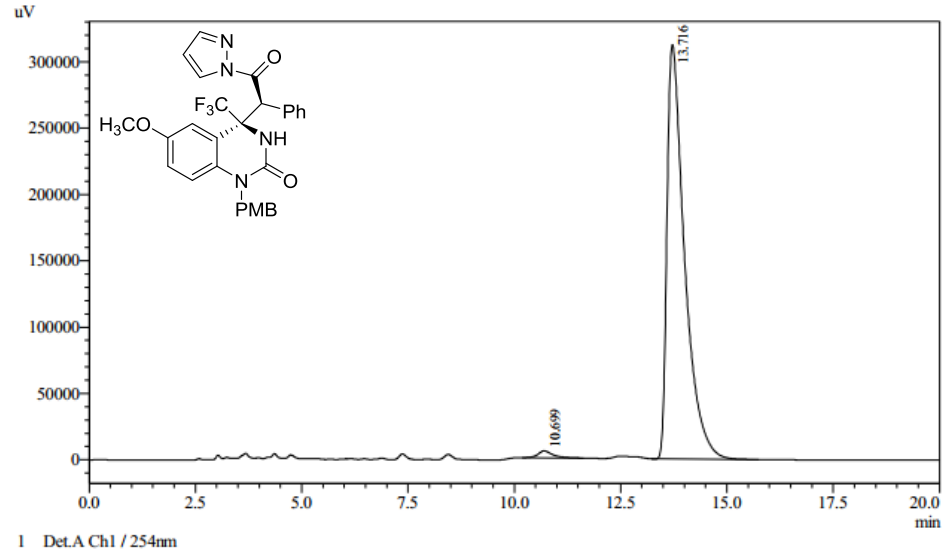
HPLC of **3q**



1 Det.A Ch1 / 254nm

Detector A Ch1 254nm

Peak#	Ret. Time	Area	Height	Area %	Height %
1	9.802	5252320	276078	16.618	19.976
2	10.576	10448633	515238	33.060	37.281
3	12.436	5553738	238558	17.572	17.261
4	13.676	10350688	352172	32.750	25.482
Total		31605378	1382047	100.000	100.000

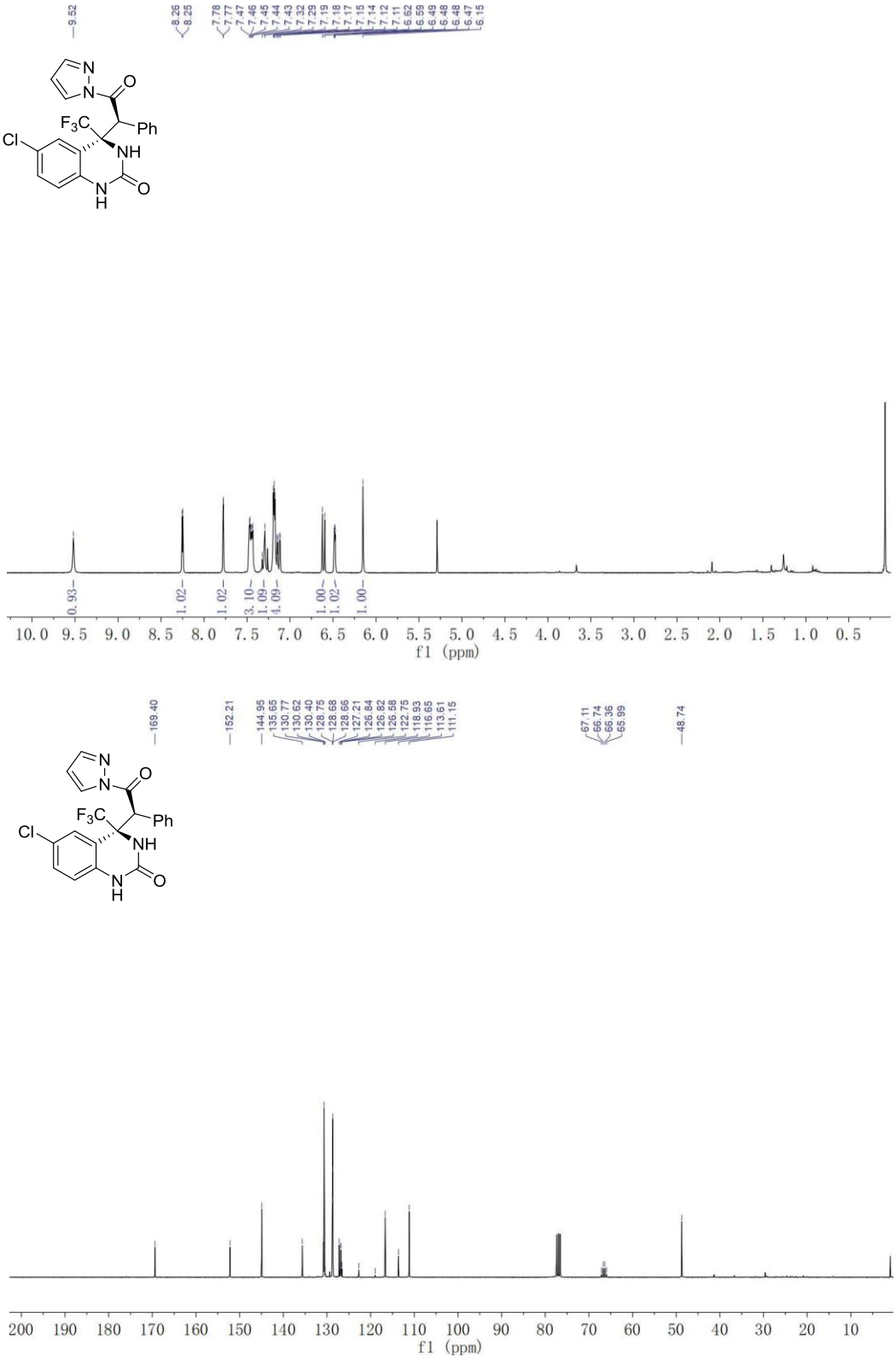


1 Det.A Ch1 / 254nm

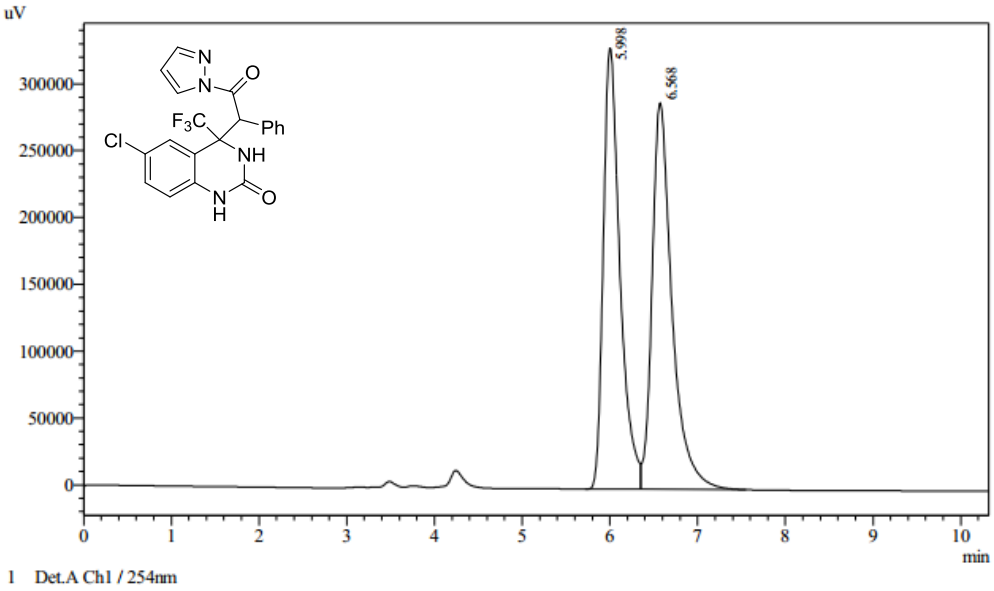
Detector A Ch1 254nm

Peak#	Ret. Time	Area	Height	Area %	Height %
1	10.699	131340	5307	1.443	1.671
2	13.716	8970682	312309	98.557	98.329
Total		9102022	317616	100.000	100.000

^{1}H and ^{13}C NMR of **4**

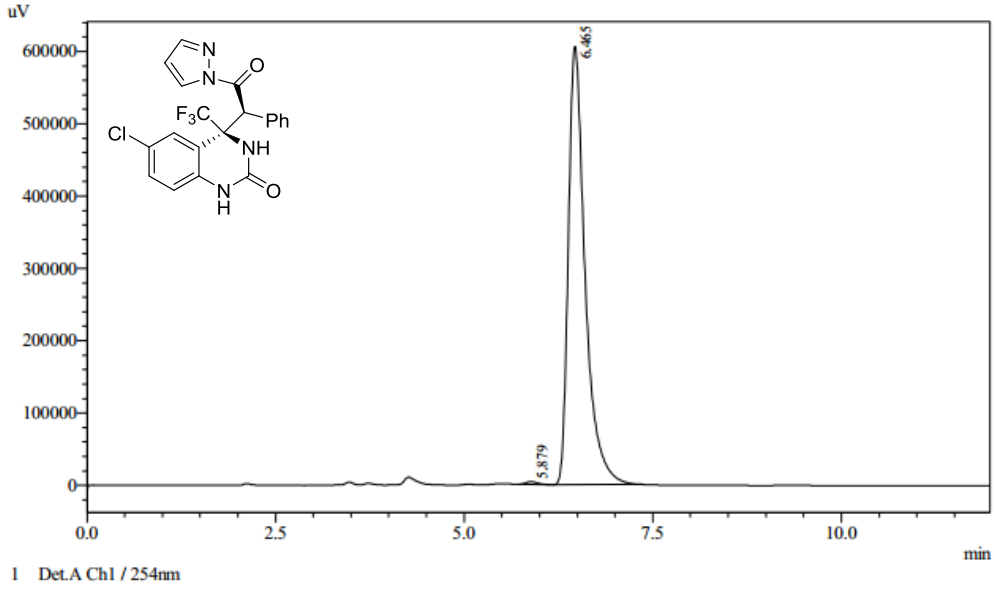


HPLC of **4**



Detector A Ch1 254nm

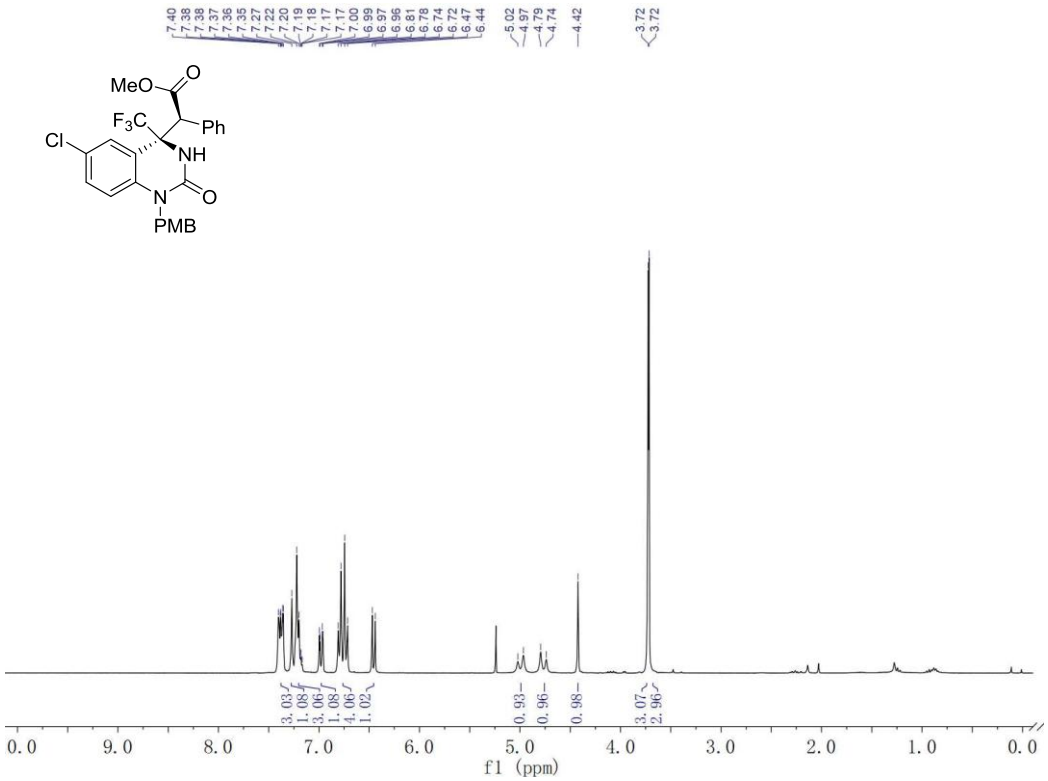
Peak#	Ret. Time	Area	Height	Area %	Height %
1	5.998	4360247	330071	48.778	53.309
2	6.568	4578683	289100	51.222	46.691
Total		8938930	619172	100.000	100.000

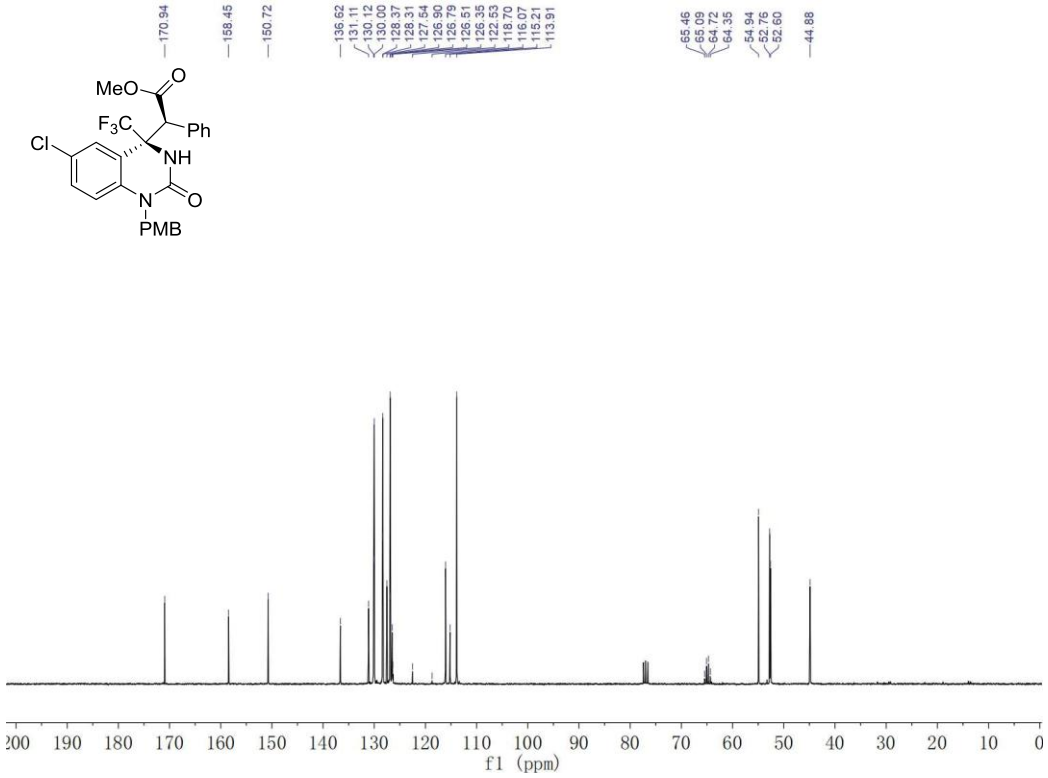


Detector A Ch1 254nm

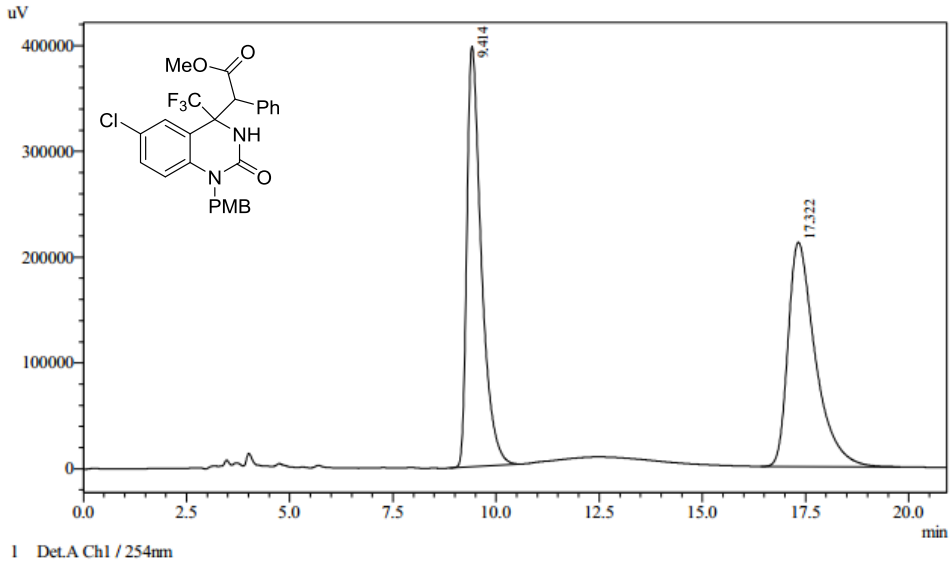
Peak#	Ret. Time	Area	Height	Area %	Height %
1	5.879	44016	3929	0.469	0.644
2	6.465	9340165	606136	99.531	99.356
Total		9384181	610065	100.000	100.000

^{1}H and ^{13}C NMR of **5**





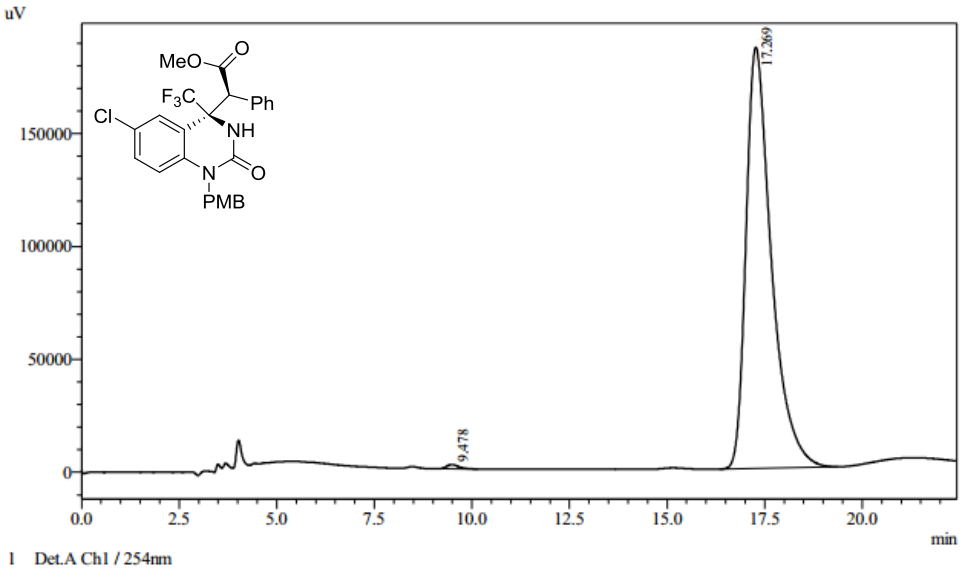
HPLC of **5**



1 Det.A Ch1 / 254nm

Detector A Ch1 254nm

Peak#	Ret. Time	Area	Height	Area %	Height %
1	9.414	9668572	397488	49.782	65.232
2	17.322	9753413	211855	50.218	34.768
Total		19421985	609343	100.000	100.000

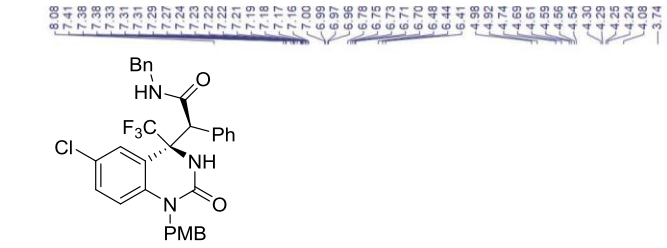


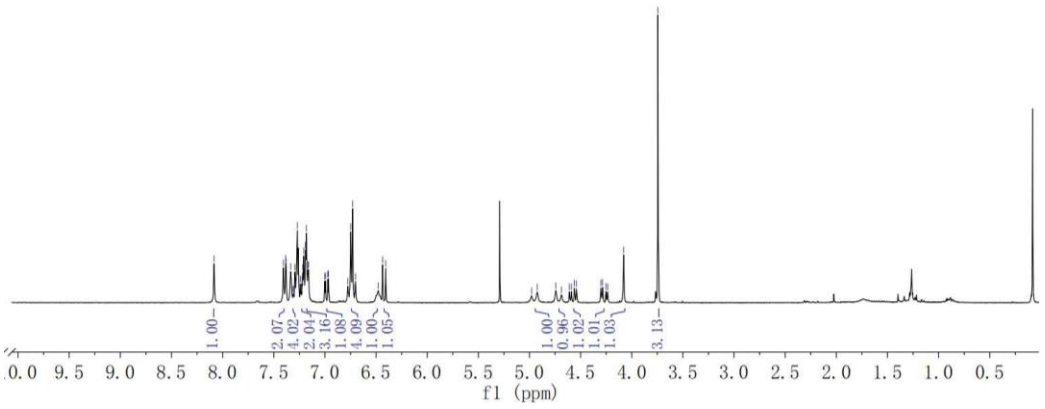
1 Det.A Ch1 / 254nm

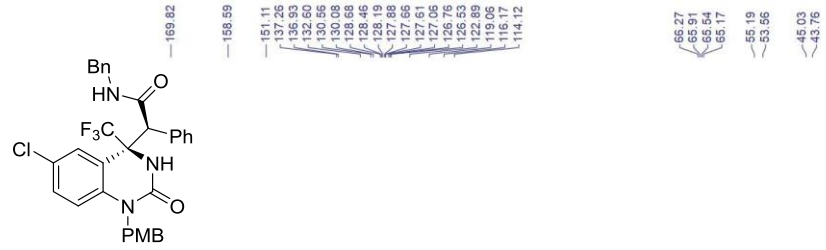
Detector A Ch1 254nm

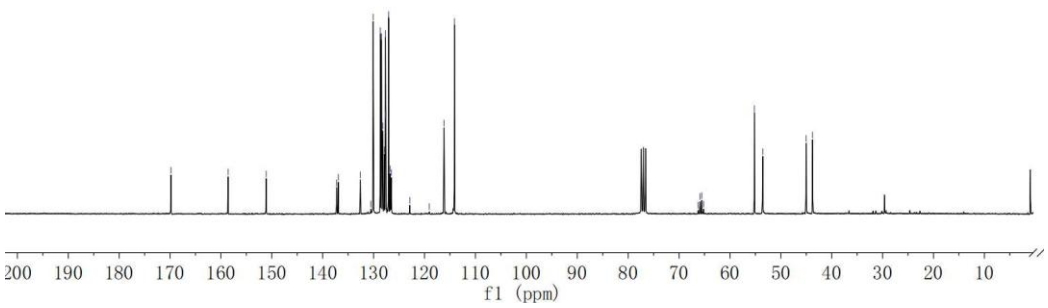
Peak#	Ret. Time	Area	Height	Area %	Height %
1	9.478	43041	1958	0.506	1.039
2	17.269	8456840	186462	99.494	98.961
Total		8499881	188420	100.000	100.000

^{1}H and ^{13}C NMR of **6**

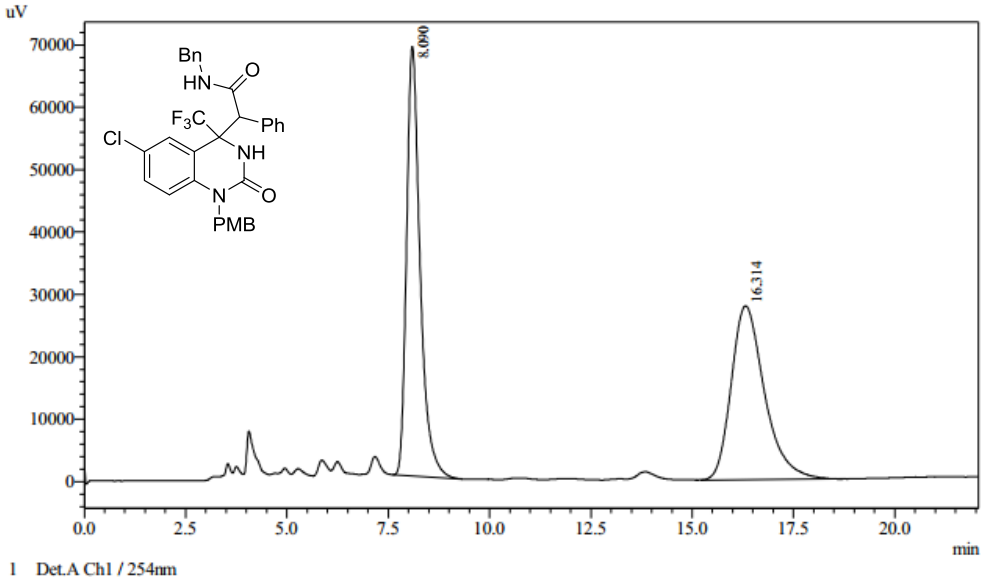








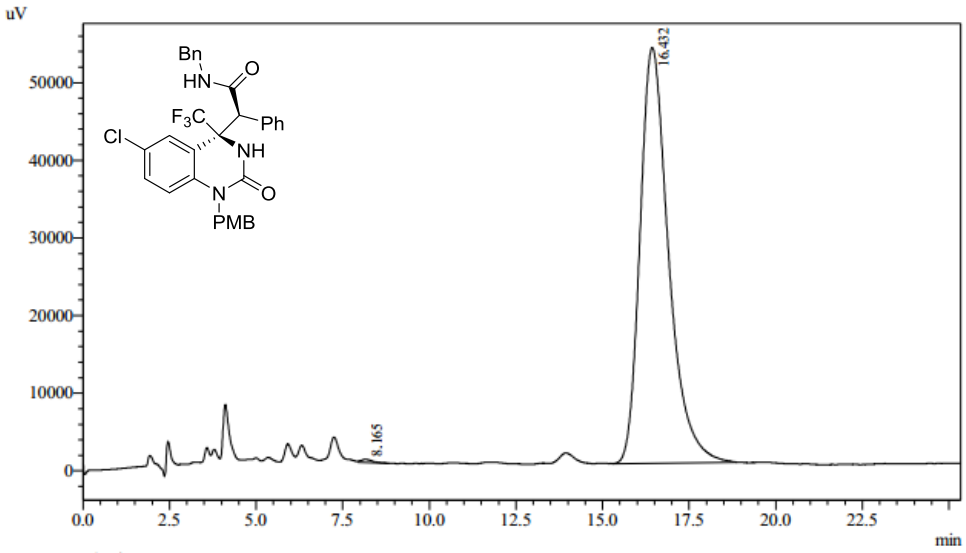
HPLC of **6**



1 Det.A Ch1 / 254nm

Detector A Ch1 254nm

Peak#	Ret. Time	Area	Height	Area %	Height %
1	8.090	1595058	68819	50.031	71.179
2	16.314	1593089	27866	49.969	28.821
Total		3188147	96685	100.000	100.000

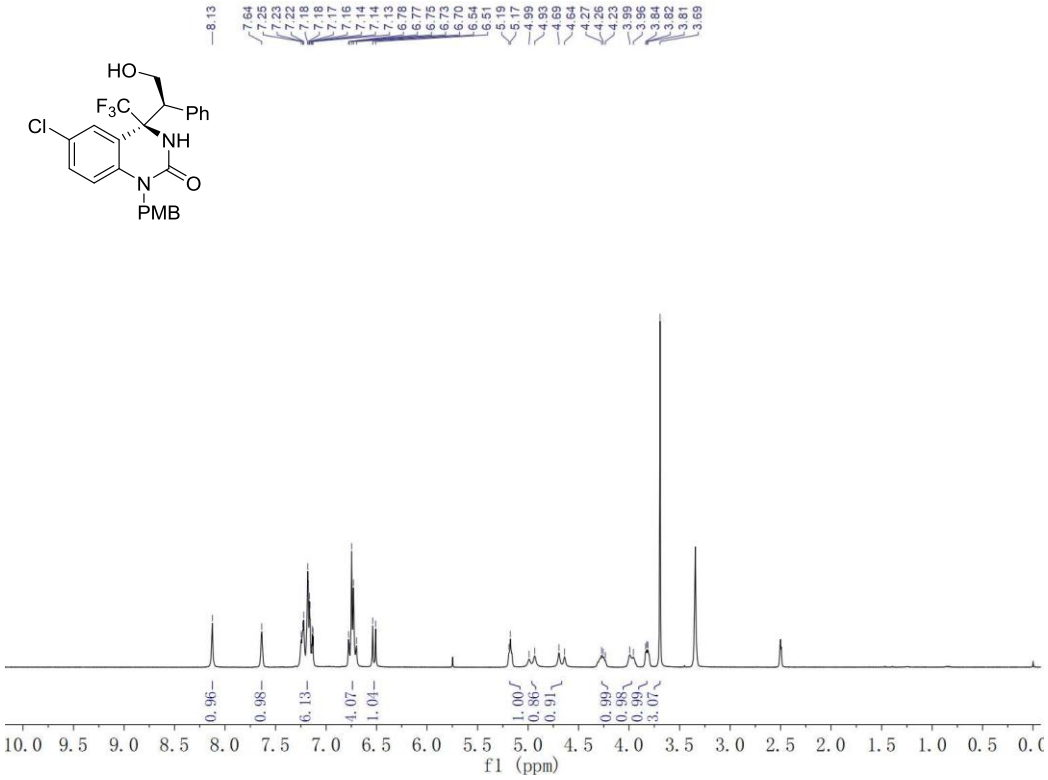


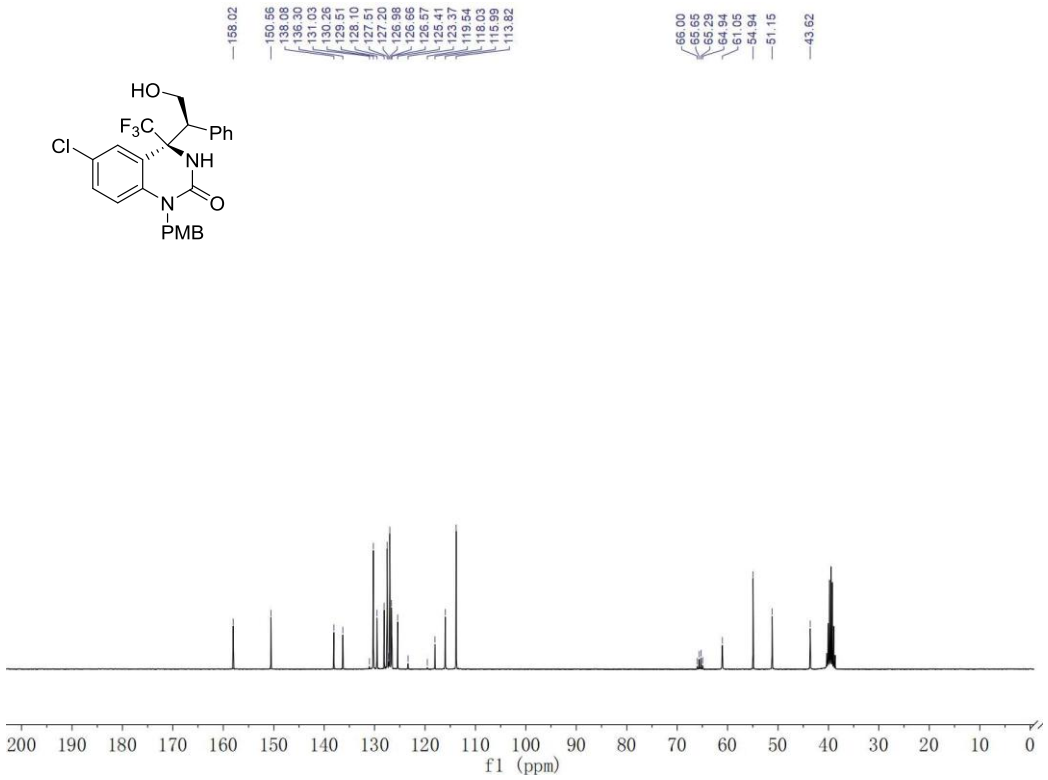
1 Det.A Ch1 / 254nm

Detector A Ch1 254nm

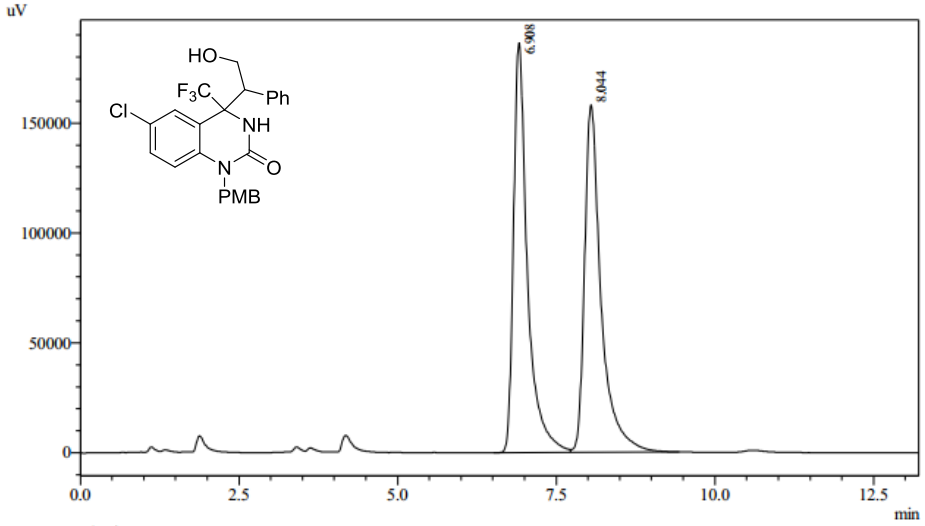
Peak#	Ret. Time	Area	Height	Area %	Height %
1	8.165	9766	421	0.317	0.780
2	16.432	3071851	53529	99.683	99.220
Total		3081617	53950	100.000	100.000

^{1}H and ^{13}C NMR of **7**





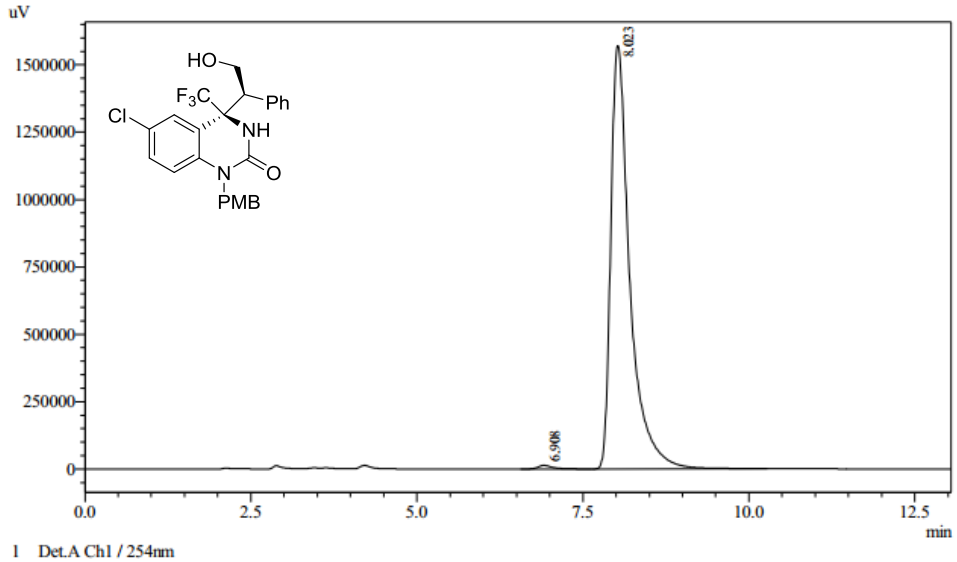
HPLC of **7**



1 Det.A Ch1 / 254nm

Detector A Ch1 254nm

Peak#	Ret. Time	Area	Height	Area %	Height %
1	6.908	2840084	186359	49.810	54.104
2	8.044	2861789	158084	50.190	45.896
Total		5701874	344444	100.000	100.000

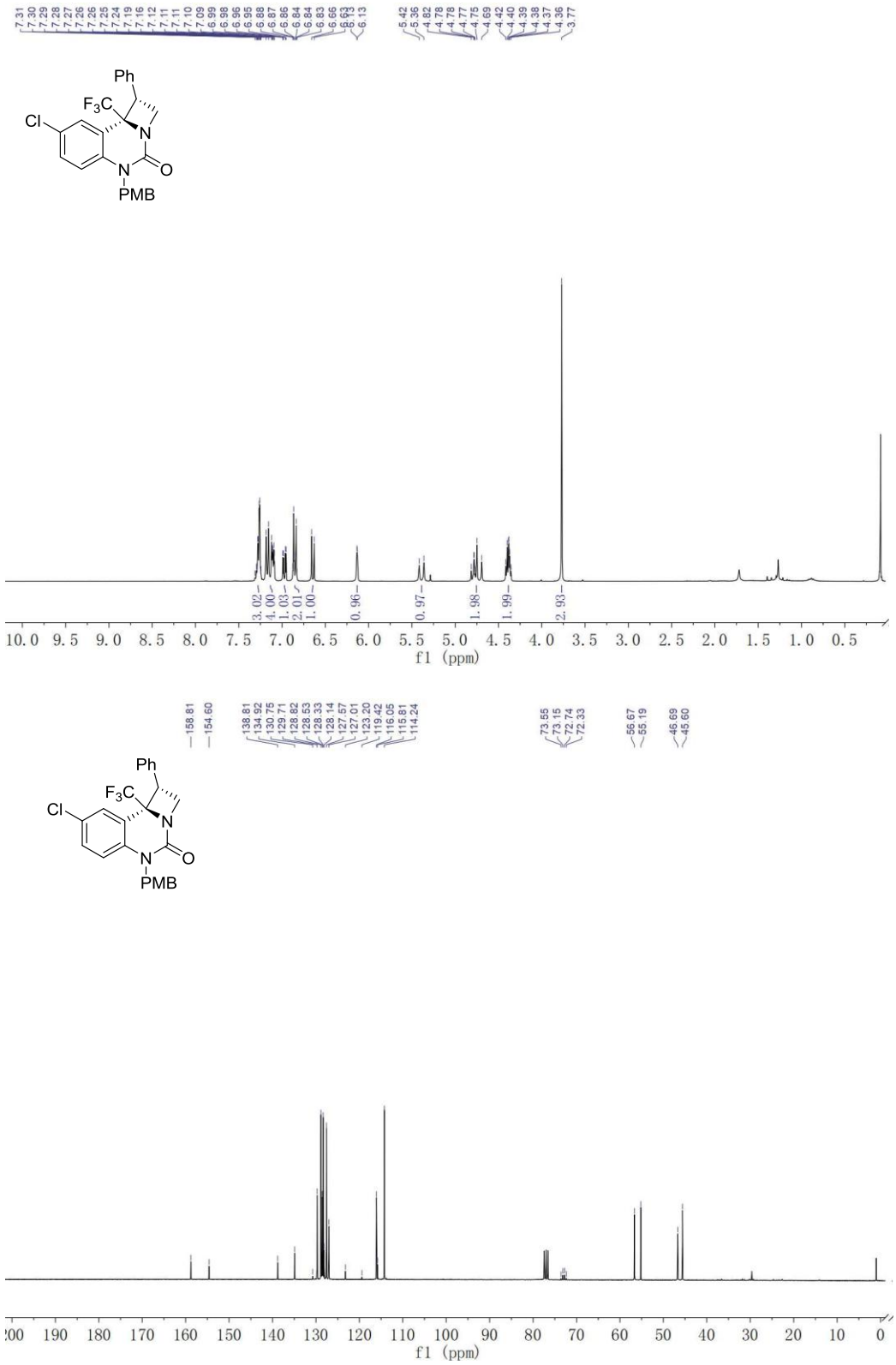


1 Det.A Ch1 / 254nm

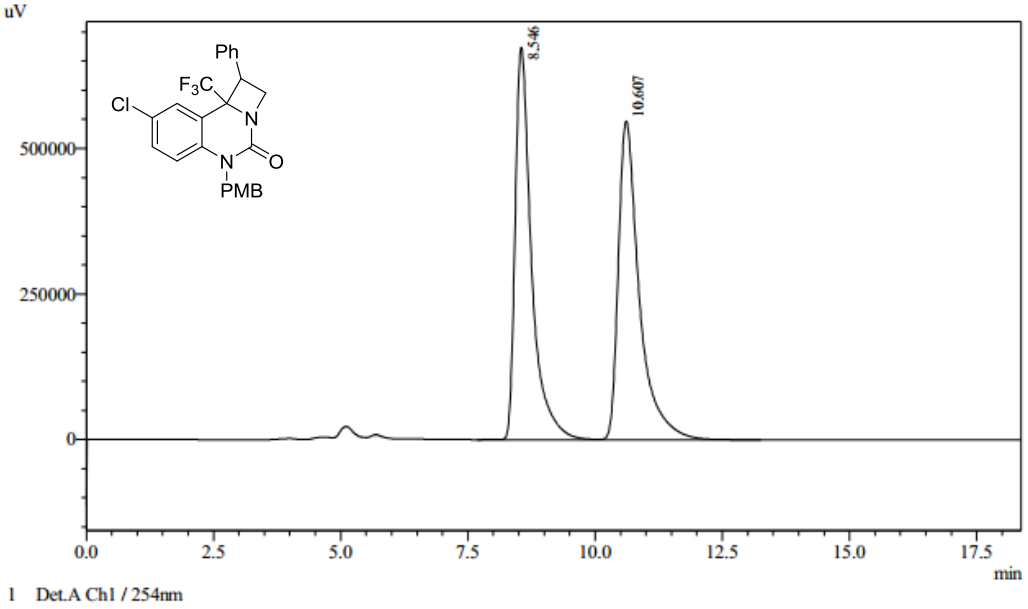
Detector A Ch1 254nm

Peak#	Ret. Time	Area	Height	Area %	Height %
1	6.908	208360	13607	0.659	0.859
2	8.023	31431261	1570331	99.341	99.141
Total		31639621	1583938	100.000	100.000

^{1}H and ^{13}C NMR of **8**



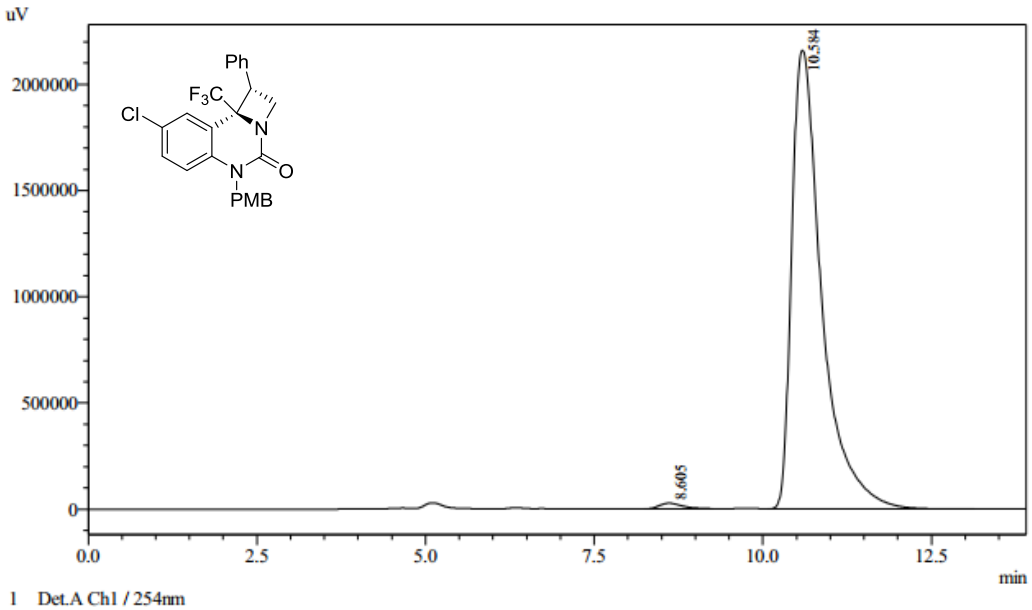
HPLC of **8**



1 Det.A Ch1 / 254nm

Detector A Ch1 254nm

Peak#	Ret. Time	Area	Height	Area %	Height %
1	8.546	15112299	674124	49.066	55.201
2	10.607	15687341	547101	50.934	44.799
Total		30799641	1221225	100.000	100.000



1 Det.A Ch1 / 254nm

Detector A Ch1 254nm

Peak#	Ret. Time	Area	Height	Area %	Height %
1	8.605	629202	26522	0.934	1.214
2	10.584	66747598	2158102	99.066	98.786
Total		67376800	2184624	100.000	100.000