Supplementary Material (ESI) for Chemical Communications

Supporting Information

Tunable DNA-Based Asymmetric Catalysis Using a G-Quadruplex Supramolecular Assembly

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Table of Contents

General Experimental

^{1}H and ^{13}C NMR spectra were recorded on a Bruker AV(III) 500 (Cryoprobe) (^{1}H at 500 MHz and ^{13}C at 125 MHz), Bruker AV(III) 400 Bruker AV 400 Bruker DPX 400 (^{1}H recorded at 400 MHz and ^{13}C recorded at 101 MHz) spectrometers. High resolution mass spectra were recorded on VG micron Autospec or Bruker microTOF. Fourier Transform Infrared Spectroscopy (FT-IR) spectra were obtained on Perkin Elmer 1600 series or Bruker Tensor 27 spectrometer. UV absorption was measured on Philips PU8720 series UV/VIS spectrometer. Thin layer chromatography was performed on Merck pre-coated silica gel plates (60F-254) or Merck aluminium backed aluminium oxide 60 F_{254} coated plates and visualised using ultraviolet light and/or $KMnO_4$ solution or *p*-anisaldehyde solution. Column chromatography was performed at ambient temperature using Merck silica gel 60 (0.063-0.200 mm) or BDH neutral aluminium oxide. THF was freshly distilled from sodium-benzophenone, dichloromethane was distilled from calcium hydride. Acetone and solid CO_2 were used to obtain a temperature of -78 ^{o}C. Where necessary, reactions requiring anhydrous conditions were performed in dry solvents in flame dried or oven-dried apparatus under nitrogen or argon atmosphere. Commercial reagents were used as received unless otherwise stated. Aza-chalcones were prepared as previously described.[1]

Procedure for DNA-Cu Catalysed Reactions

An Eppendorf containing a solution of preformed *h*-Tel or *c*-kit quadruplex solution (210 μL, 240 μM in buffer, 0.3 eq (buffer = 50 mM MOPS buffer, pH 6.5, 150 mM KCl)) was taken out of the freezer and thawed at room temperature for 1 h. Next, a preformed solution of the ligand-Cu complex (145 μL, 268 μM, 0.24 eq) was added and the mixture agitated for a few seconds on a vortex mixer. A solution of the chalcone substrate (50 μL, 3.33 mM in MeCN, 1 eq) was then added and the mixture agitated again on a vortex mixer. Finally, the reaction was cooled to 5 ˚C and additional buffer was added (90 μL) followed by a solution of freshly cracked cyclopentadiene (5 μL, 1M in MeCN, 30 eq). The mixture was then stirred at 5 ºC by continuous inversion for 3 days. At 24h and 48h, additional freshly cracked cyclopentadiene (5 μL, 1M in MeCN, 30 eq.) was added.

The contents of the Eppendorf were extracted with diethyl ether (3 times), and the combined extracts dried ($MgSO_4$), filtered, then evaporated. The resulting residue was then dissolved in requisite HPLC eluent (45 μL) along with the internal standard solution (biphenyl 3.16127 mM in 1% IPA:heptane, 5 μL) and analysed by chiral HPLC.

Experimental Methods for CD Studies and Tabulated Results

Human telomeric (*h*-Tel) DNA refers to the sequence, 5'-(AGGGTTAGGGTTAGGGTTAGGG)
c-kit promoter quadruplex '*c*-kit 87up'(*c*-kit) refers to the sequence, 5'-(AGGGAGGGCGCTGGGAGGAGGG)

Method:

CD spectra were recorded on an Applied Photophysics Pi-Star-180 Spectrophotometer interfaced with an Acorn Archimedes computer with inbuilt software (Applied Photophysics Ltd, Surrey UK). The optical system was configured with a 75 W Xe lamp, circular light polarizer and end mounted photomultiplier. The machine had previously been calibrated with (D)-camphorsulfonic acid. The temperature was regulated using a Neslab RTE-300 circulating programmable water bath (Neslab Inc.) and a thermoelectric temperature controller (Melcor).

DNA at 5.1 μM or 2.6 μM (*h*-Tel and *c*-kit respectively) in KCl (100 mM) potassium phosphate (10 mM, pH = 7) were unfolded at 368 K equilibrated for around 30 min before being annealed by decreasing the temperature to 298 K at a rate ~ 0.2 K/min. The ellipticity was recorded at 260 nm (*c*-kit) and 290 nm (*h*-Tel) at 0.5 K intervals.

CD spectra were recorded at 298 K in a 10 mm path length cell over a wavelength range of 216-340 nm in steps of 1 nm, with 3 nm entrance/exit slit widths; the number of counts was set to 10,000 with adaptive sampling set to 500,000. The spectra were corrected by subtracting the spectrum of the same buffer solution.

CD spectra were recorded on annealed *h*-Tel and *c*-kit and on *h*-Tel and *c*-kit which were annealed in the presence of up to 50 μM of either **2** or **4**.

Annealing data were fitted to a 2 state equilibrium folding model in Igor^{TM} (V 5.0.5.7 WaveMetrics) giving good fits to the data allowing determination of the T_m and ΔH for the folding transition from which ΔS and ΔG_{298} were calculated from $\Delta G = \Delta H - T\Delta S$.

Table S1 Folding thermodynamic parameters calculated for *h*-Tel, *c*-kit and their complexes with **2** and **4**.

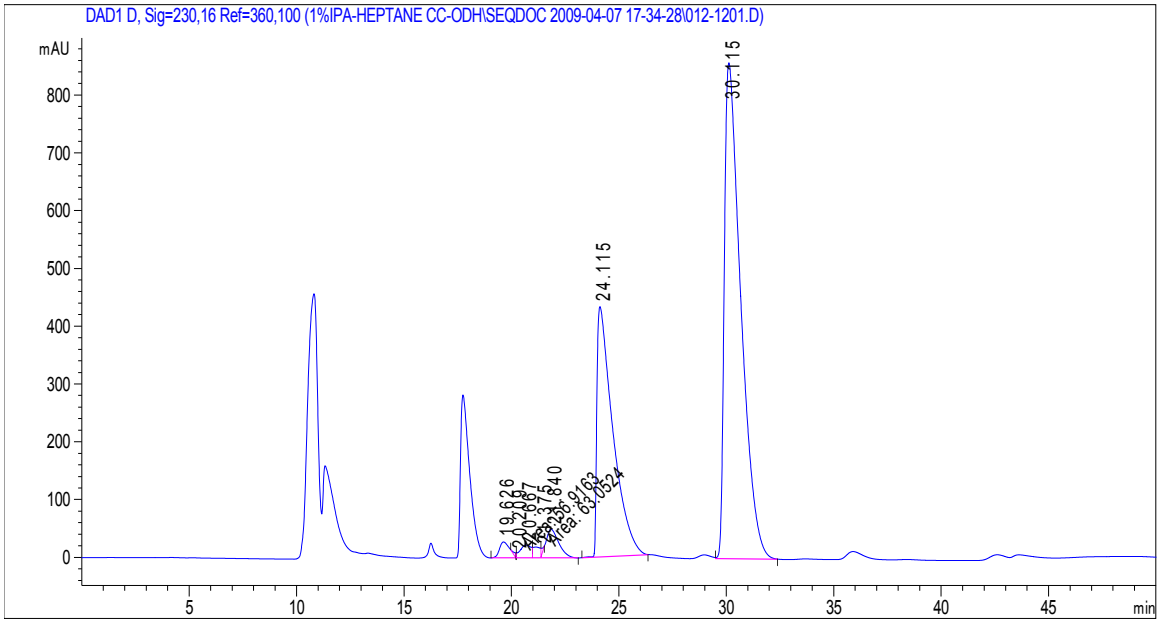
	T_m (+-) /K	ΔH (+-) /kJmol^{-1}	ΔS /Jmol^{-1}	ΔG_{298} /Jmol^{-1}	ΔT_m /K
c-kit	339.53 (0.08)	184 (2.16)	541.4838	22487.82	-
c-kit + **2**	339.79 (0.10)	204 (3.45)	600.724	25104.25	0.26
c-kit + **4**	340.98 (0.10)	185 (2.71)	540.1197	23214.34	1.45
h-Tel	342 (0.5)	190 (1.16)	555.4386	24439.3	-
h-Tel + **2**	344. 5 (0.06)	193 (1.45)	560.529	26057.55	2.5
h-Tel + **4**	344.3 (0.05)	199 (1.36)	579.4946	26830.6	2.3

Experimental Details for HPLC

HPLC data was collected with Agilent Technologies 1200 Series hardware using either a Daicel Chemical Industries Ltd. Chiracel® OD-H column (4.6 mm ø × 250 mm) in experiments involving aza-chalcone **5**, or a Daicel Chemical Industries Ltd. Chiralpak® AD column (4.6 mm ø × 250 mm) in experiments involving aza-chalcone **6**. For aza-chalcone **5**, 1% IPA in heptane was used as the eluent, eluting over a 50 min period at 30 ˚C at a rate of 0.5 mL/min. For aza-chalcone **6,** 2% IPA in heptane was used as the eluent, eluting over a 90 min period at 30 ˚C at a rate of 0.5 mL/min. All solvents were HPLC grade and purchased from Fisher Scientific and used as received.

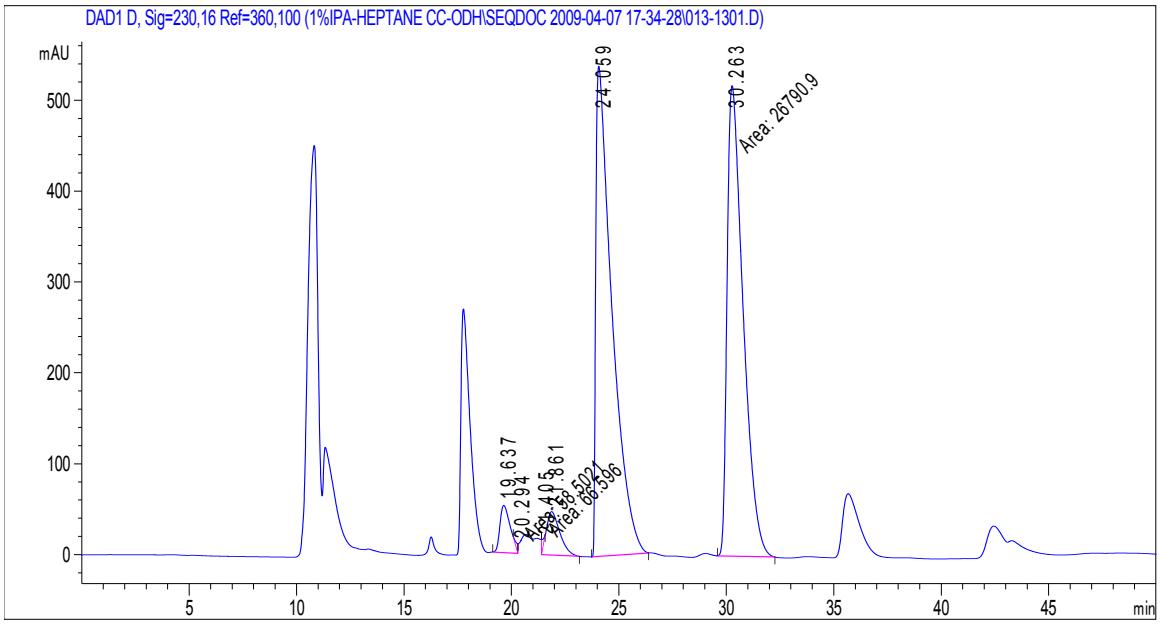
HPLC Traces

Ligand **1**, aza-chalcone **5**, *h*-Tel.



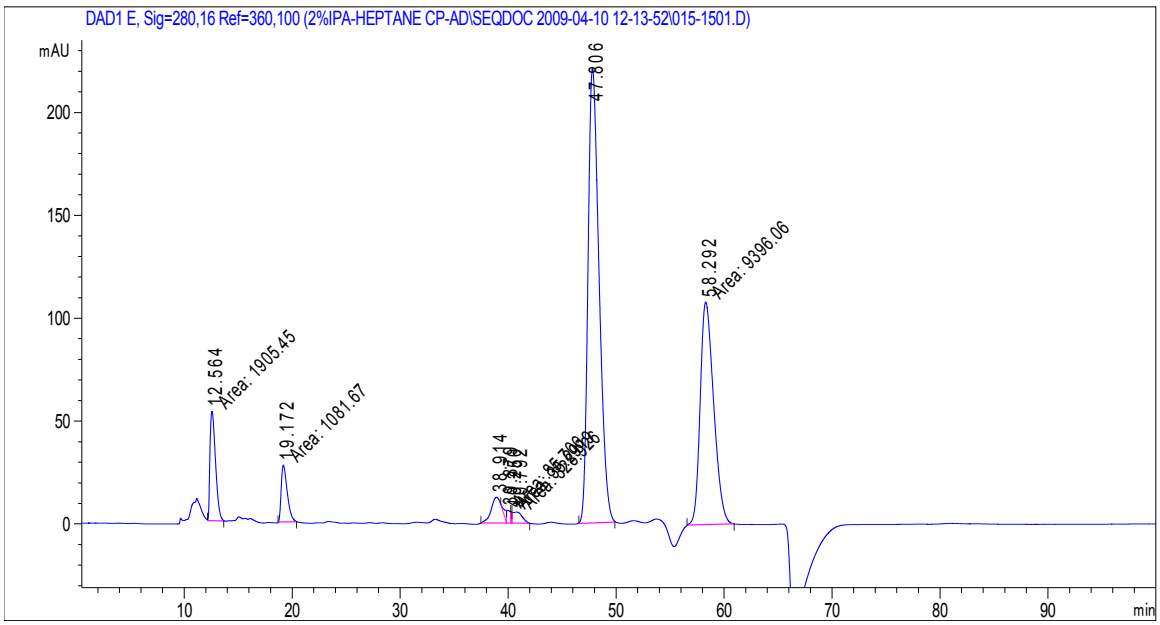
#	Time	Area	Height	Width	Area%	Symmetry
1	19.626	908.1	27.7	0.492	1.254	0
2	20.209	56.9	8.6	0.1107	0.079	0
3	20.667	789.7	22.4	0.518	1.090	1.124
4	21.375	63.1	16.4	0.0643	0.087	0
5	21.84	2479.3	49.6	0.7391	3.423	0
6	24.115	22415.5	433.1	0.7418	30.946	0.217
7	30.115	45721.8	858.5	0.7934	63.122	0.349

Ligand **1**, aza-chalcone **5**, *c*-kit.



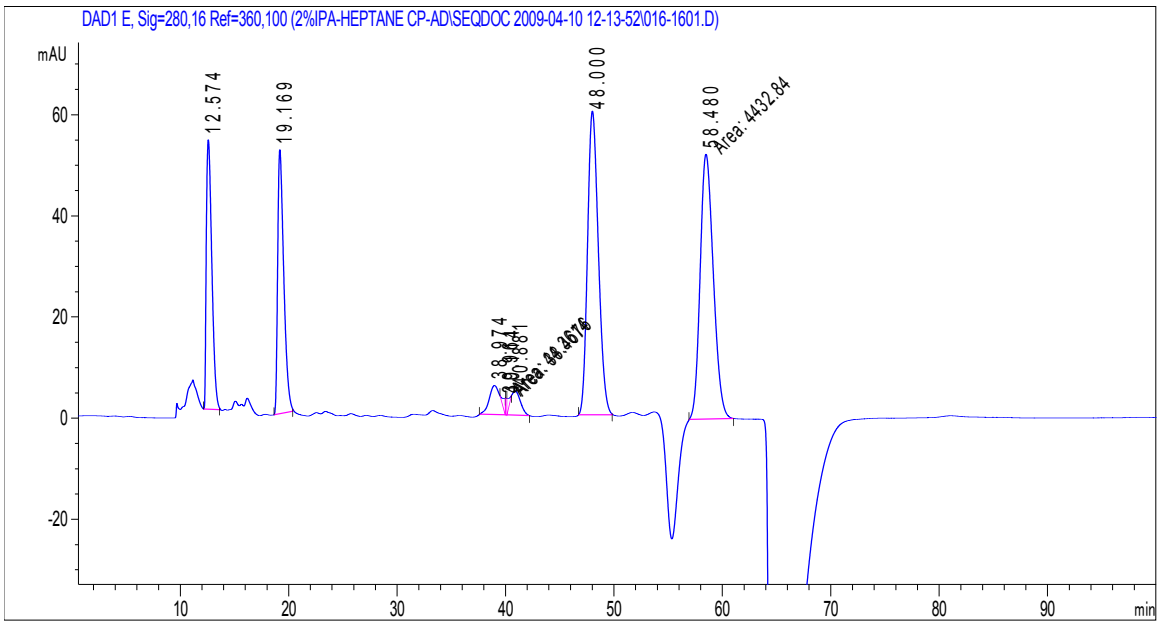
#	Time	Area	Height	Width	Area%	Symmetry
1	19.637	1731	52.2	0.5032	2.935	0
2	20.294	58.5	0.3	0.0943	0.099	0
3	21.405	66.6	16.7	0.0666	0.113	0
4	21.861	2084.2	7.9	0.647	3.534	0
5	24.059	28251.3	539.4	0.7431	47.898	0.202
6	30.263	26790.9	517.9	0.8621	45.422	0.432

Ligand **1**, aza-chalcone **6**, *h*-Tel.



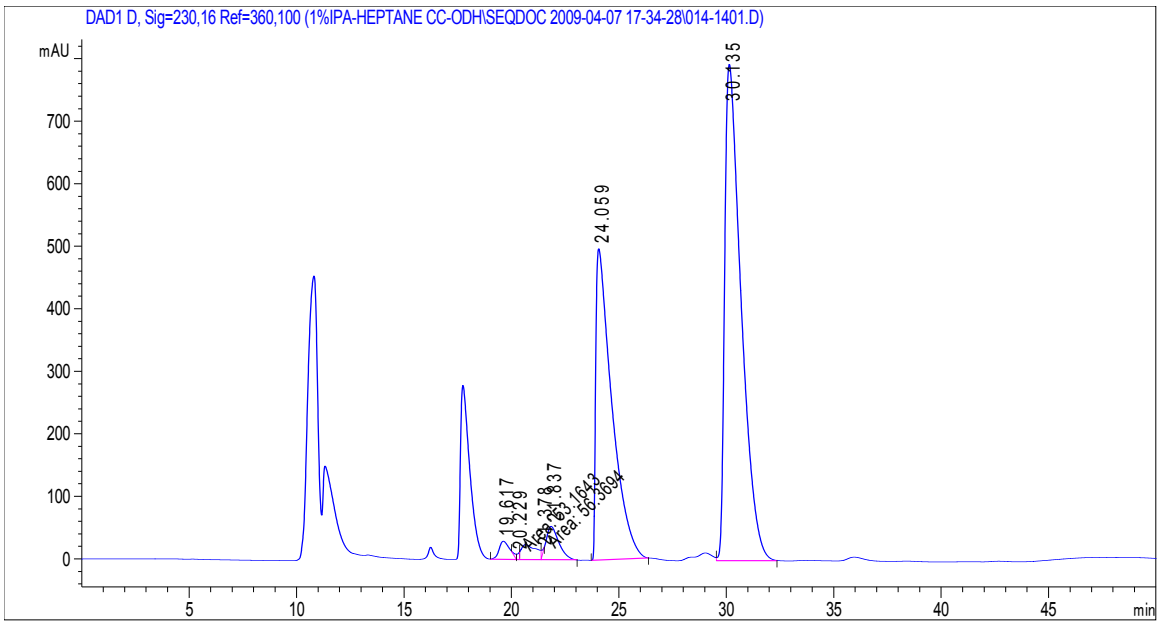
#	Time	Area	Height	Width	Area%	Symmetry
1	12.564	1905.4	53.3	0.5963	6.525	0.55
2	19.172	1081.7	27.8	0.6493	3.704	0.528
3	38.914	596.3	12.6	0.7879	2.042	0
4	39.879	85.7	6.4	0.2242	0.293	0
5	40.25	35.3	5.5	0.1071	0.121	0
6	40.792	328.9	5.5	1.004	1.126	0.693
7	47.806	15773.4	221.2	1.1	54.013	0.647
8	58.292	9396.1	108.2	1.4468	32.175	0.677

Ligand **1**, aza-chalcone **6**, *c*-kit.



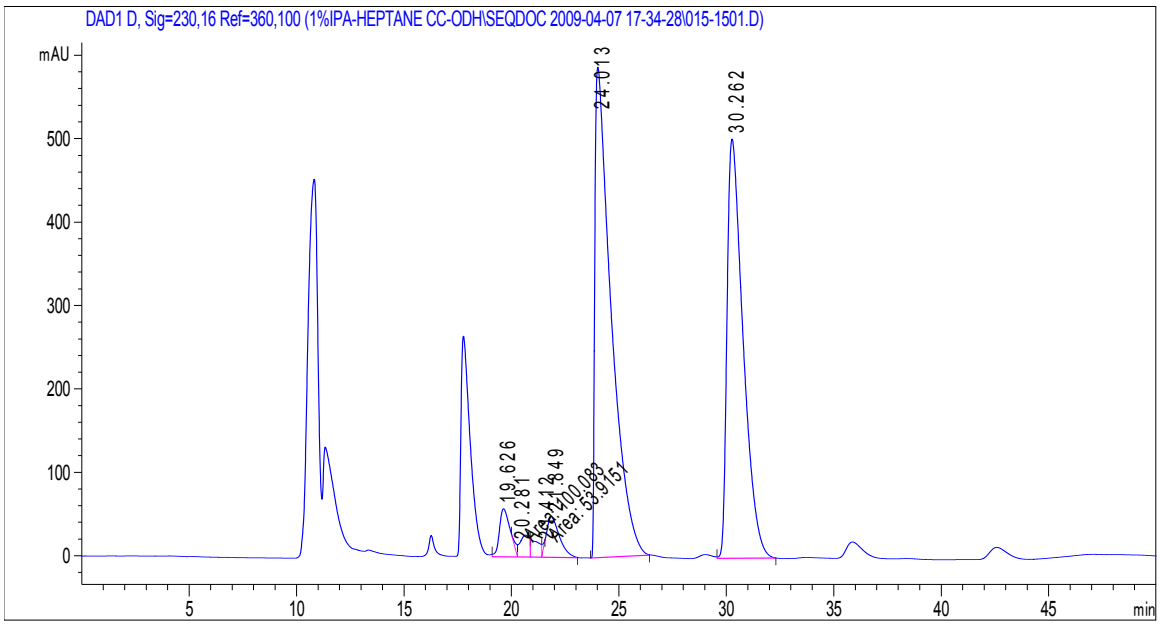
#	Time	Area	Height	Width	Area%	Symmetry
1	12.574	1882.1	53.3	0.55	14.104	0.532
2	19.169	2038.8	52.2	0.5973	15.278	0.507
3	38.974	408.1	5.8	1.1751	3.058	0
4	39.961	44.4	3.4	0.2207	0.332	0
5	40.114	38.5	3.4	0.1892	0.288	0
6	40.881	327.5	4.8	1.1356	2.455	0
7	48	4172.4	60.1	1.0678	31.267	0.777
8	58.48	4432.8	52.4	1.4095	33.218	0.771

Ligand **2**, aza-chalcone **5**, *h*-Tel.



#	Time	Area	Height	Width	Area%	Symmetry
1	19.617	1077.5	29.1	0.6172	1.484	0
2	20.229	53.2	8.3	0.1071	0.073	0
3	21.378	56.4	15	0.0627	0.078	0
4	21.837	3348	53.6	1.0407	4.610	0
5	24.059	25873.8	498	0.7381	35.624	0.207
6	30.135	42220.9	794.1	0.7903	58.132	0.359

Ligand **2**, aza-chalcone **5**, *c*-kit.



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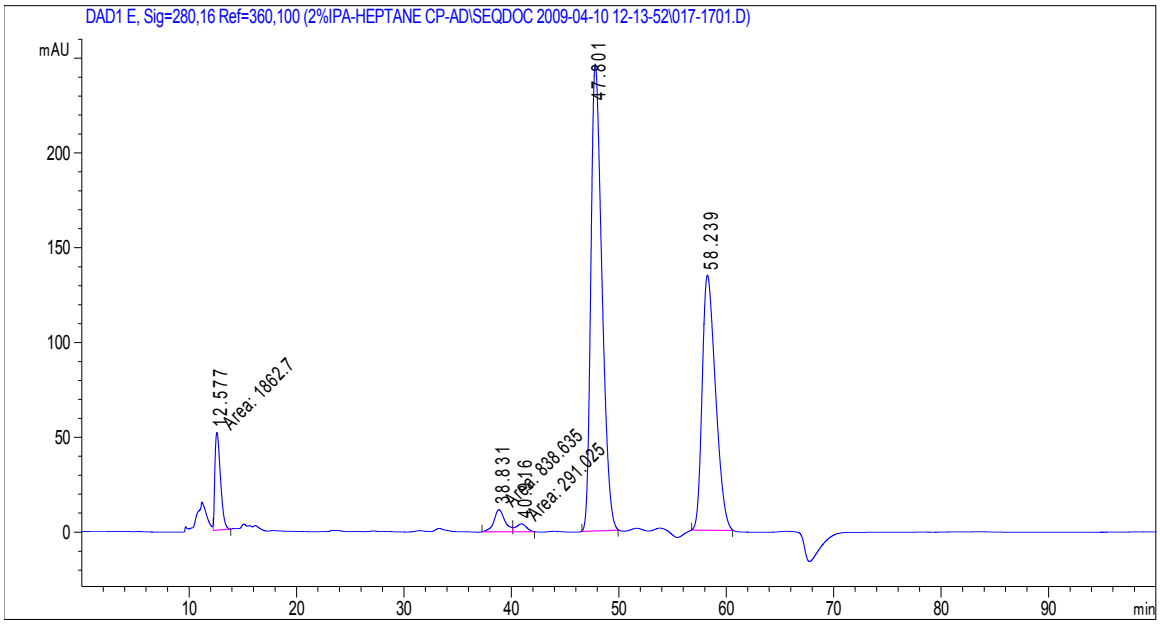
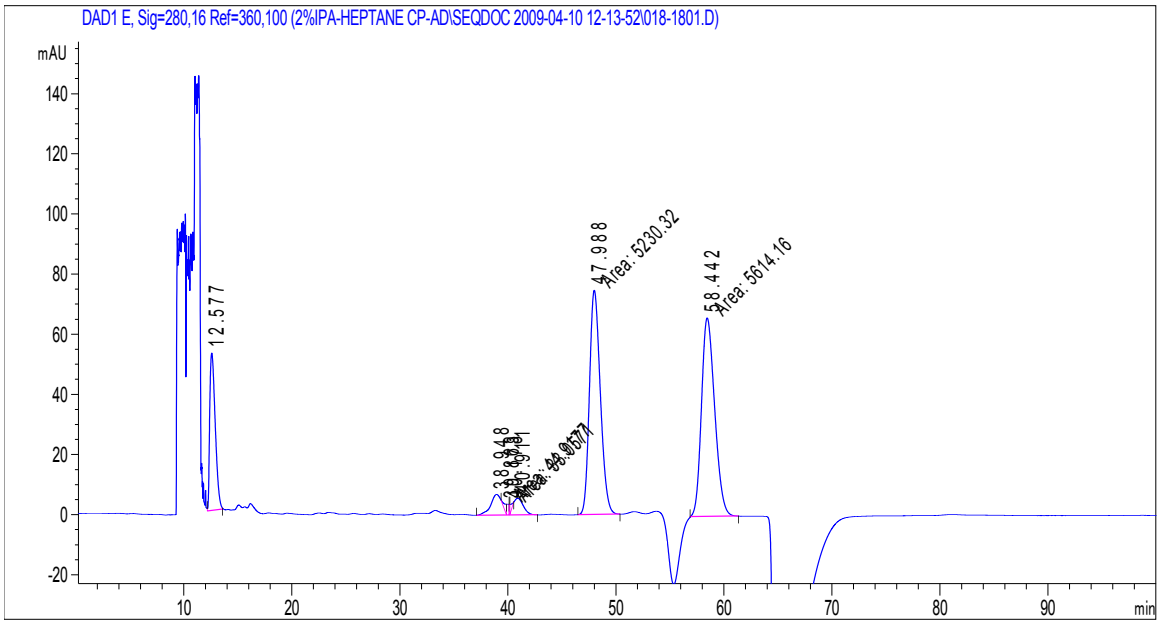
1	19.626	2778.7	57.7	0.8023	4.430	0
2	20.281	100.1	14.6	0.114	0.160	0
3	21.412	53.9	15.4	0.0584	0.086	0
4	21.849	2663.1	49.1	0.9047	4.246	0
5	24.013	31028.9	588	0.7496	49.472	0.198
6	30.262	26095.6	502.8	0.7815	41.606	0.42

Ligand **2**, aza-chalcone **6**, *h*-Tel.



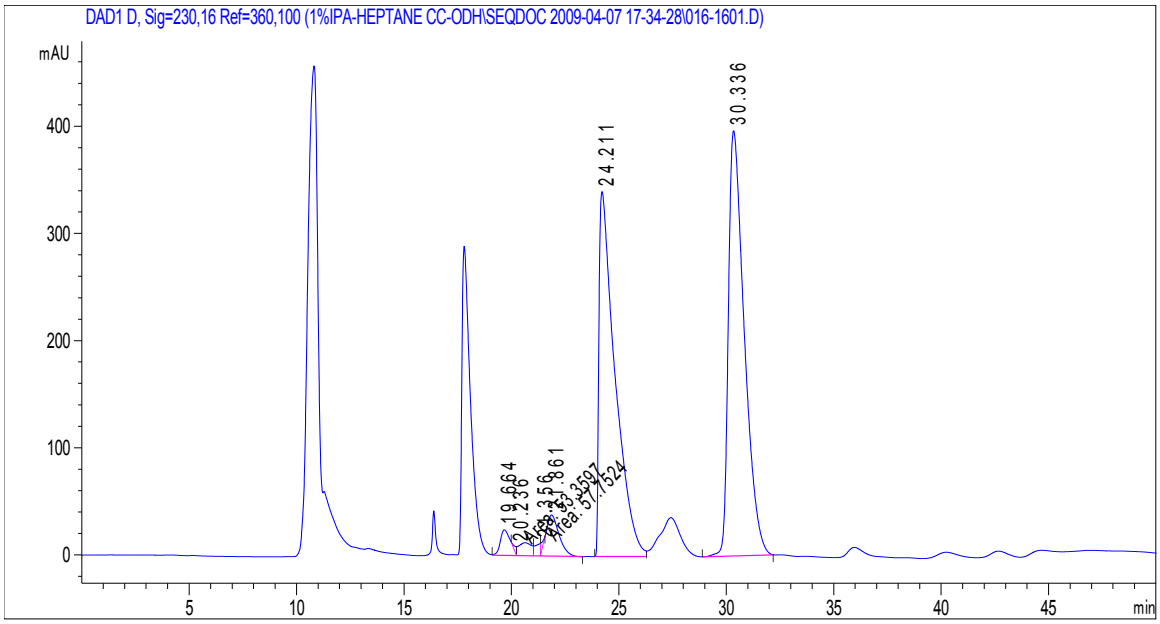
#	Time	Area	Height	Width	Area%	Symmetry
1	12.577	1862.7	51.6	0.6018	5.766	0.543
2	38.831	838.6	11.7	1.1919	2.596	0.832
3	40.916	291	4.2	1.1463	0.901	1.027
4	47.801	17631.5	246.5	1.0926	54.576	0.63
5	58.239	11682.3	134.7	1.322	36.161	0.619

Ligand **2**, aza-chalcone **6**, *c*-kit.



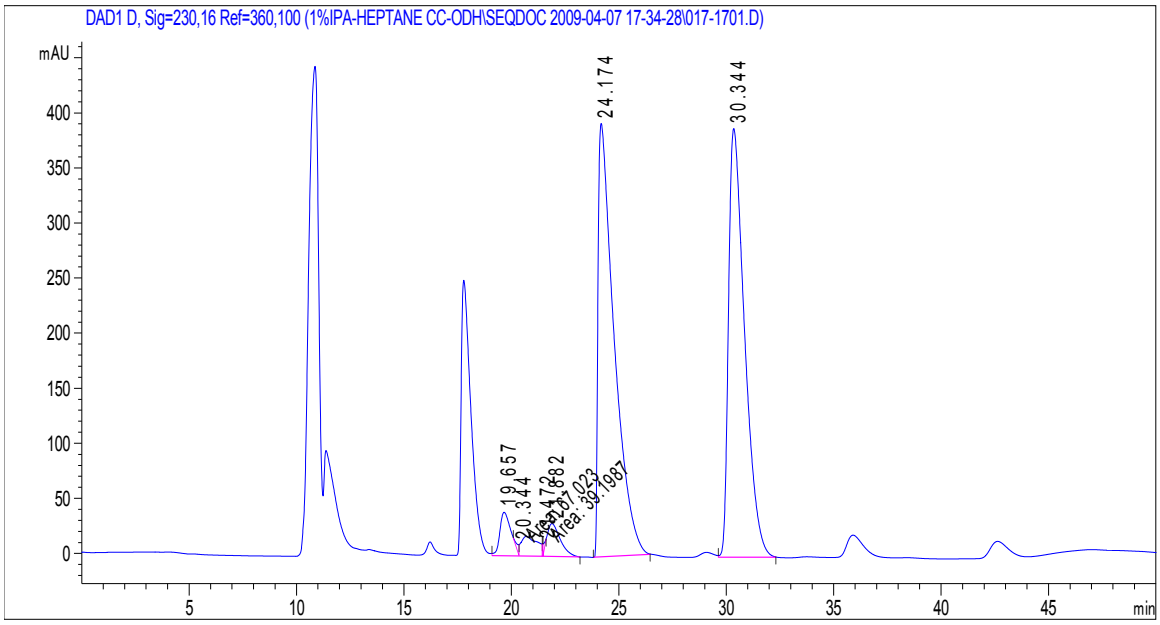
#	Time	Area	Height	Width	Area%	Symmetry
1	12.577	1859.4	52.4	0.5558	13.567	0.543
2	38.948	543.6	6.9	1.3152	3.967	0
3	39.863	44.9	3.4	0.2171	0.328	0
4	40.178	33.1	3.4	0.1622	0.241	0
5	40.911	379.3	5.6	1.13	2.768	0
6	47.988	5230.3	74.6	1.1685	38.164	0.773
7	58.442	5614.2	66	1.4172	40.965	0.744

Ligand **3**, aza-chalcone **5**, *h*-Tel.



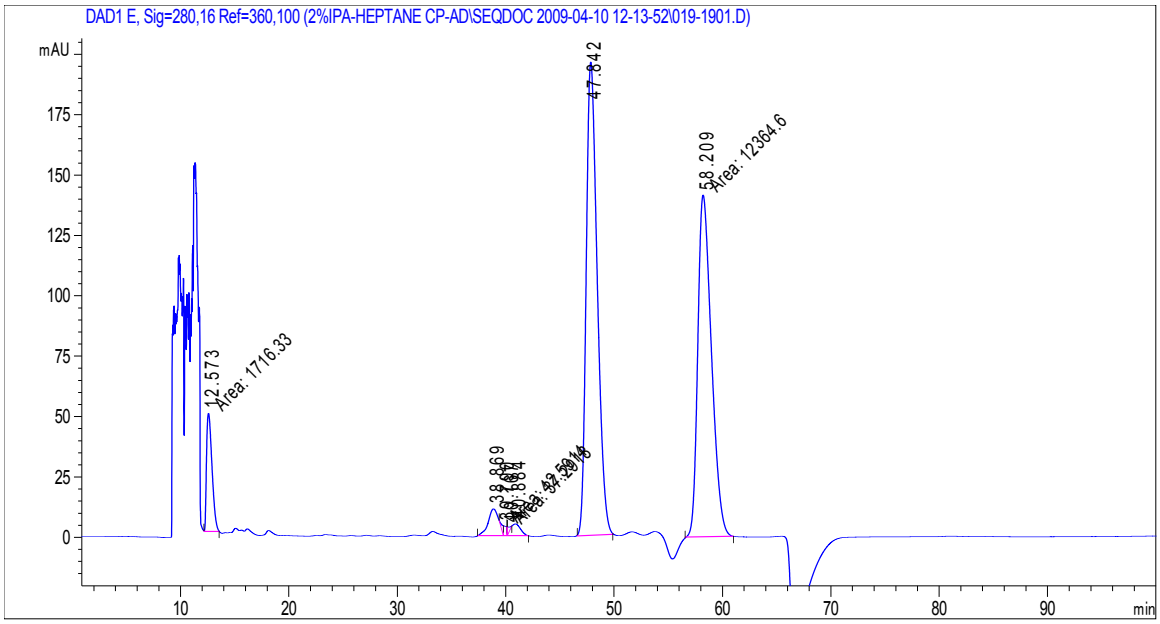
#	Time	Area	Height	Width	Area%	Symmetry
1	19.664	1280.6	23.9	0.7919	3.093	0
2	20.236	53.4	8.3	0.1073	0.129	0
3	21.356	57.8	11.6	0.0832	0.139	0
4	21.861	1830.6	38.6	0.6789	4.421	0
5	24.211	17719.5	340.7	0.7329	42.794	0.214
6	30.336	20464.4	396.9	0.7756	49.423	0.463

Ligand **3**, aza-chalcone **5**, *c*-kit.



#	Time	Area	Height	Width	Area%	Symmetry
1	19.657	2379.7	39.7	0.8944	5.340	0
2	20.344	67	10	0.1118	0.150	0
3	21.472	39.2	11.3	0.0579	0.088	0
4	21.882	1323.9	30	0.6462	2.971	0
5	24.174	20531.6	393.6	0.7486	46.069	0.219
6	30.344	20225.4	389.2	0.7862	45.382	0.448

Ligand **3**, aza-chalcone **6**, *h*-Tel.



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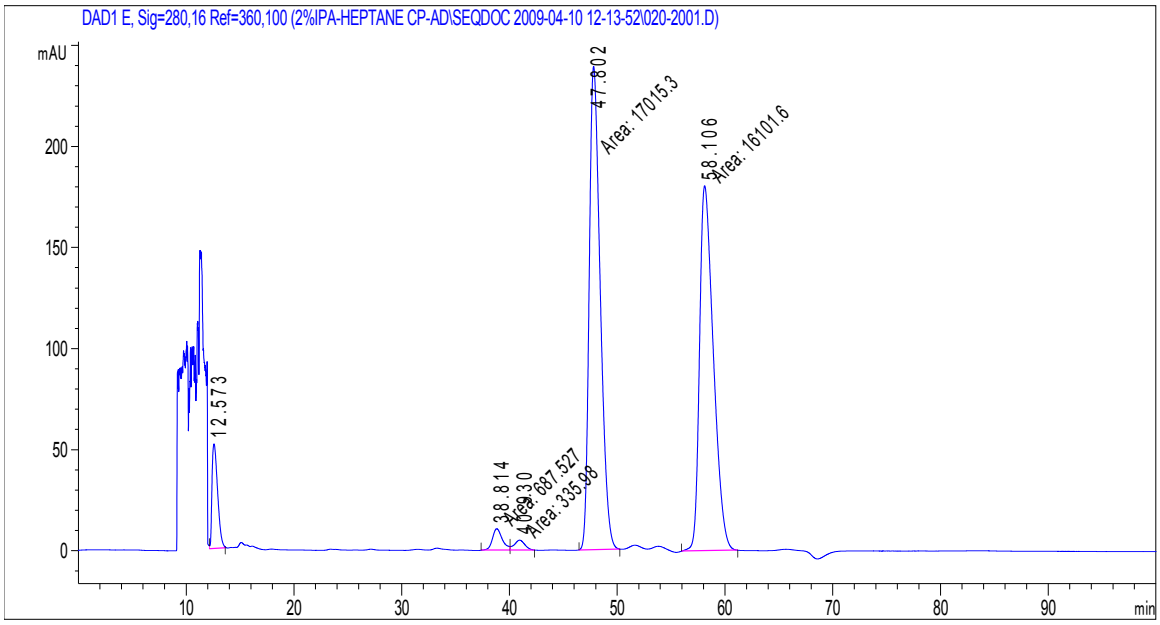
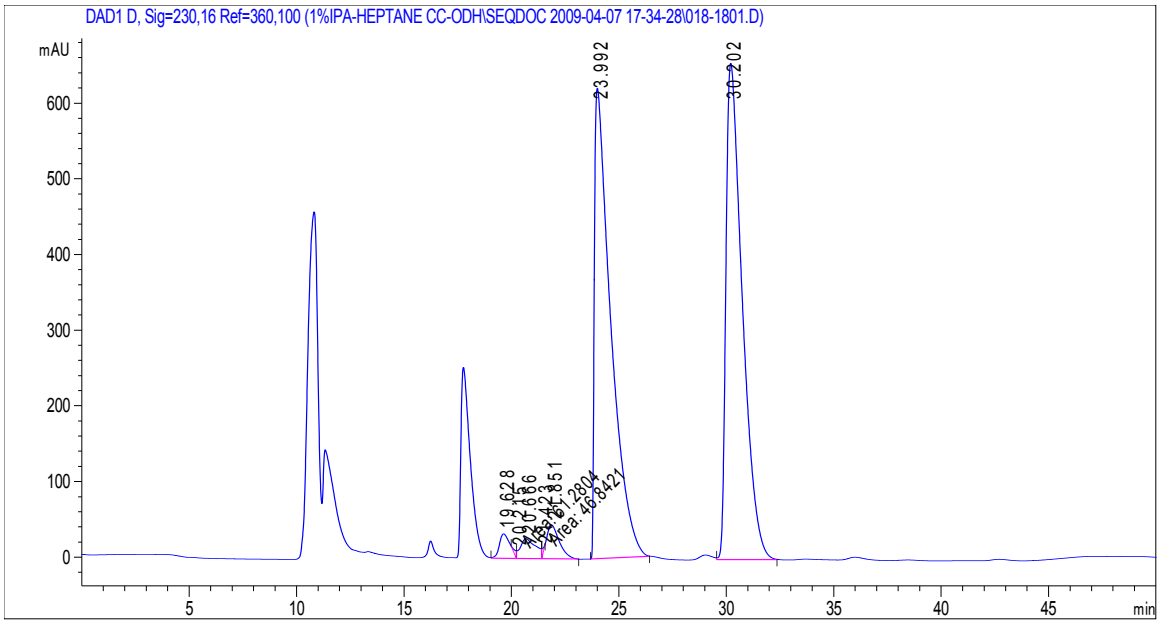
1	12.573	1716.3	48.9	0.5844	5.885	0.543
2	38.869	821.8	11.2	1.2266	2.818	0
3	39.79	42.6	4	0.179	0.146	0
4	40.167	37.3	3.5	0.1787	0.128	0
5	40.884	315.3	4.9	1.0669	1.081	0
6	47.842	13867.6	196	1.0854	47.548	0.664
7	58.209	12364.6	141.6	1.4557	42.395	0.622

Ligand **3**, aza-chalcone **6**, *c*-kit.



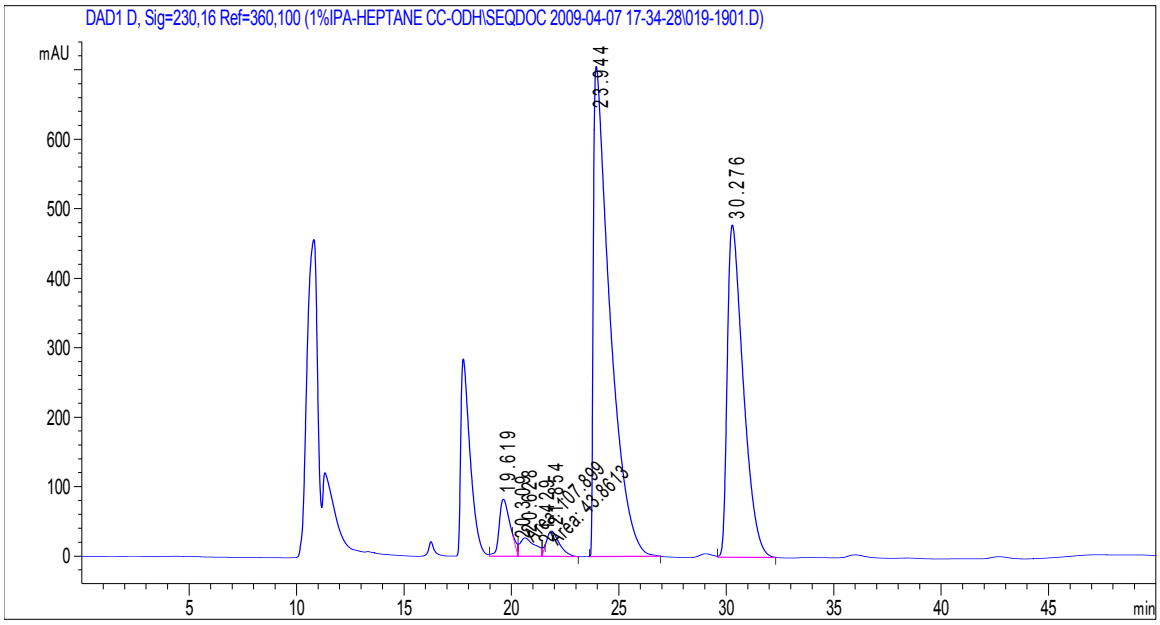
#	Time	Area	Height	Width	Area%	Symmetry
1	12.573	1872.9	51.7	0.5623	5.201	0.524
2	38.814	687.5	10.7	1.0751	1.909	0.763
3	40.93	336	5	1.1287	0.933	0.987
4	47.802	17015.3	239.2	1.1858	47.247	0.646
5	58.106	16101.6	180.6	1.4859	44.710	0.574

Ligand **4**, aza-chalcone **5**, *h*-Tel.



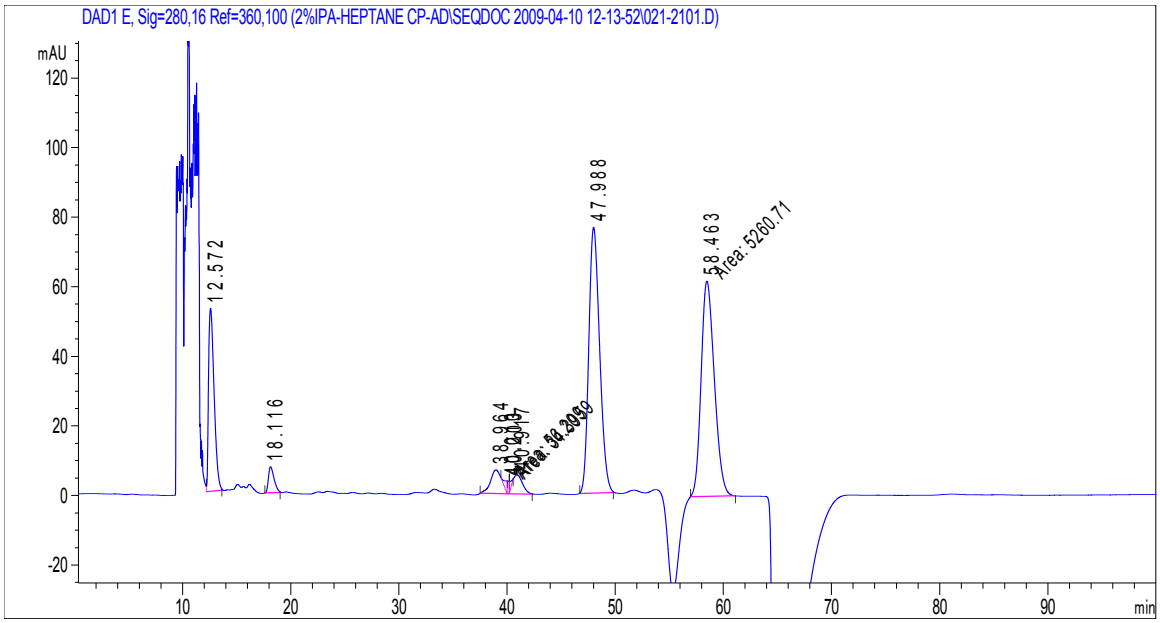
#	Time	Area	Height	Width	Area%	Symmetry
1	19.628	1110.8	32.4	0.4847	1.541	0
2	20.215	61.3	9.5	0.1075	0.085	0
3	20.666	1279.8	26.2	0.6793	1.776	0.534
4	21.423	46.8	13.4	0.0583	0.065	0
5	21.851	1882	45.1	0.6175	2.612	0
6	23.992	32976.9	621.9	0.7506	45.762	0.195
7	30.202	34704.6	656.2	0.789	48.159	0.383

Ligand **4**, aza-chalcone **5**, *c*-kit.



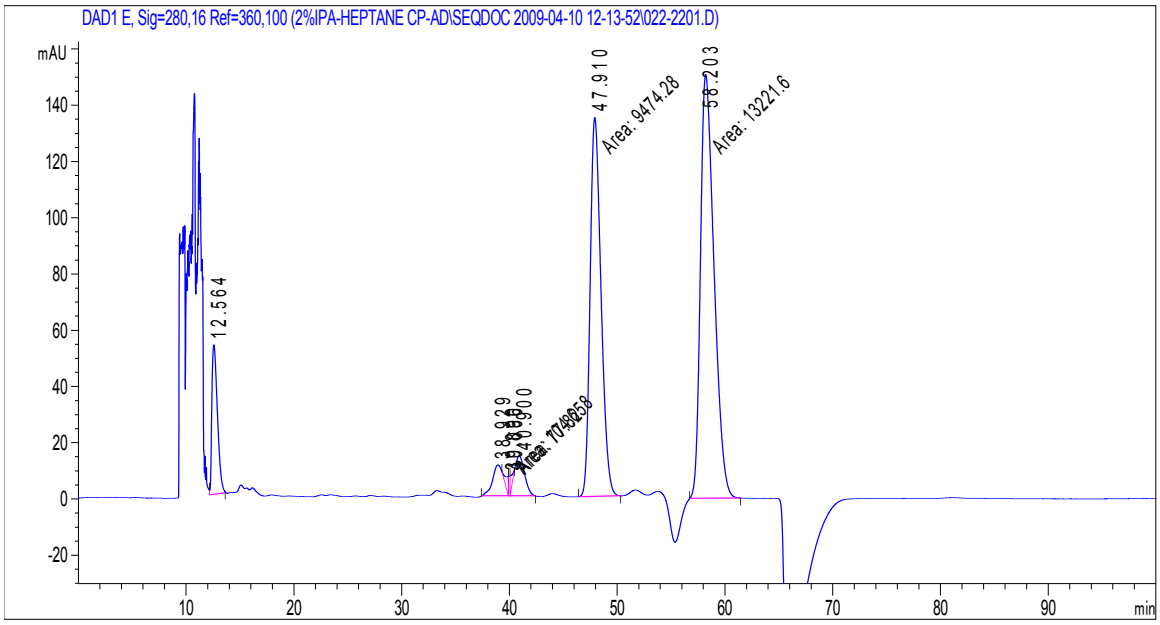
#	Time	Area	Height	Width	Area%	Symmetry
1	19.619	2889.2	82.5	0.5281	4.213	0
2	20.309	107.9	16.9	0.1061	0.157	0
3	20.628	1291.5	26.7	0.6674	1.883	0.447
4	21.429	43.9	12.4	0.0589	0.064	0
5	21.854	1542.8	36.9	0.6161	2.250	0
6	23.944	37900.1	705.6	0.7567	55.264	0.188
7	30.276	24804.5	478.8	0.7804	36.169	0.426

Ligand **4**, aza-chalcone **6**, *h*-Tel.



#	Time	Area	Height	Width	Area%	Symmetry
1	12.572	1880.5	52.7	0.5566	13.727	0.528
2	18.116	272.1	7.5	0.5288	1.986	0.561
3	38.964	528	6.8	1.2881	3.854	0
4	40.01	56.2	3.7	0.2525	0.410	0
5	40.203	34.4	3.6	0.1192	0.251	0
6	40.917	345.4	5.5	1.0478	2.521	0
7	47.988	5321.7	76.4	1.0683	38.848	0.762
8	58.463	5260.7	61.9	1.4164	38.402	0.749

Ligand **4**, aza-chalcone **6**, *c*-kit.



#	Time	Area	Height	Width	Area%	Symmetry
1	12.564	1910	53.2	0.5571	7.188	0.529
2	38.929	781.2	11.1	1.1745	2.940	0
3	39.89	104.7	6.9	0.2531	0.394	0
4	40.066	77.8	7.3	0.1773	0.293	0
5	40.9	1002.5	14.3	1.1683	3.773	0
6	47.91	9474.3	134.8	1.1718	35.655	0.718
7	58.203	13221.6	150.7	1.4622	49.758	0.605

References

[1] S. Otto, F. Bertoncin and J. B. F. N. Engberts, *J. Am. Chem. Soc.,* 1996, **118**, 7702.