SUPPLEMENTAL MATERIAL

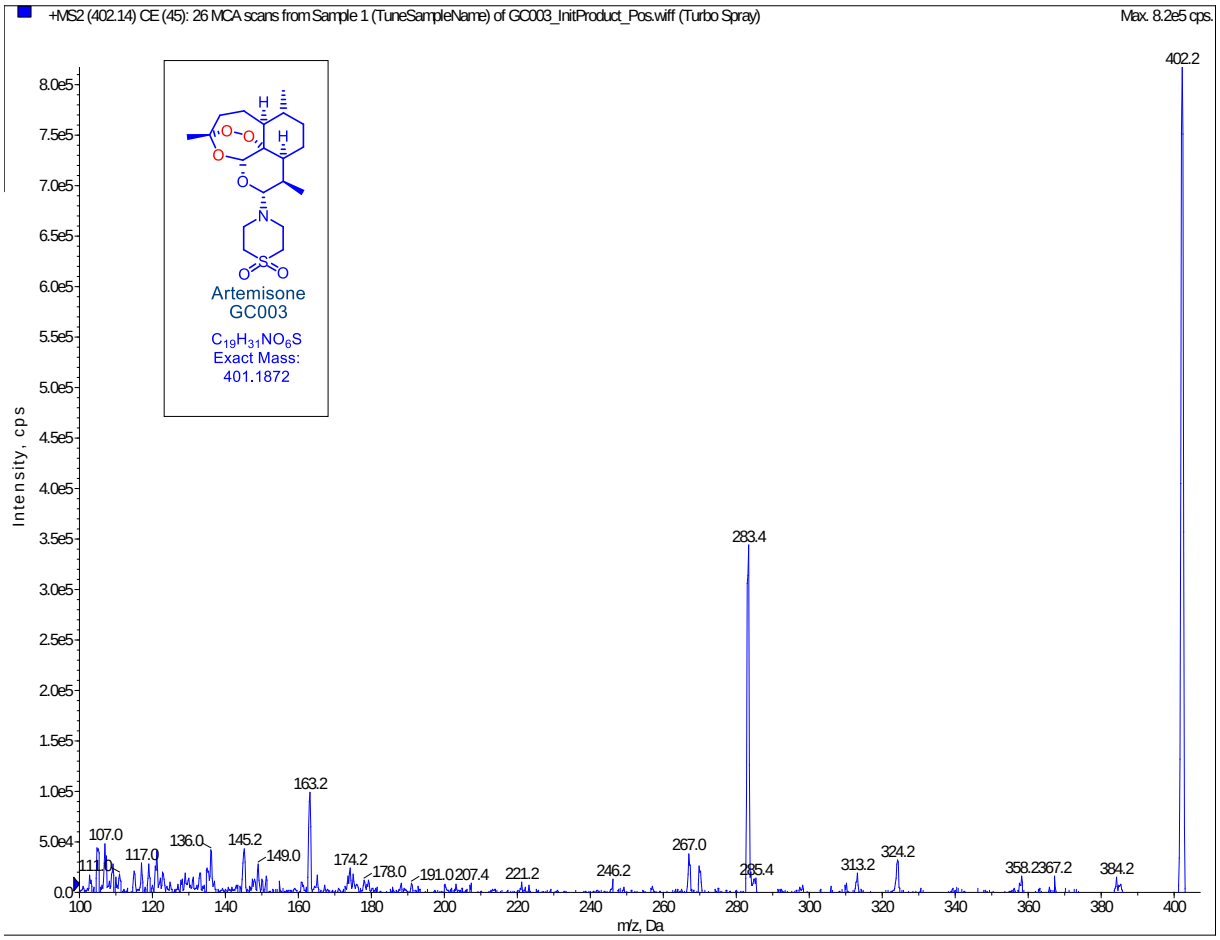
Part 1: Chemistry experimental details

^{1}H-NMR and ^{13}C NMR spectra were recorded on solutions in $CDCl_3$ with a Bruker AV 400 spectrometer operating at 400 MHz (HKUST) or a Bruker Avance^{TM} III spectrometer operating at 600 MHz (NWU). Chemical shifts (δ) are reported in parts per million (ppm); ^{1}H chemical shifts are reported downfield of tetramethylsilane (TMS) with internal reference to the residual proton in $CDCl_3$ (δ 7.25 ppm). ^{13}C chemical shifts were internally referenced to the $CDCl_3$ resonances (δ 77.00 ppm). The splitting patterns are abbreviated as follows: s (singlet), d (doublet), dd (doublet of doublets), t (triplet) and m (multiplet). Infrared spectra of solid samples were obtained from KBr disks on an FT-IR Perkin-Elmer Spectrum One spectrometer. Melting points were recorded on a Leica Microscope Heating Stage 350 and are corrected (HKUST). Mass spectra were recorded on an API QSTAR high performance triple quadrupole time-of-flight mass spectrometer with electrospray ionization, and on a Waters Micromass GCT Premier Mass Spectrometer operating in CI mode, with NH_3 as the CI reagent gas (HKUST) or on a Bruker MicroTOF Q II mass spectrometer, equipped with an ESI source set at 180 °C using Bruker Compass DataAnalysis 4.0 software (NWU). At the Division of Clinical Pharmacology, University of Cape Town (UCT), each of the samples in hand at UCT, namely artemisone, artemiside, 10-sulfamide, 10-arylamine, and 10-phenylurea (Fig. 2, text), and the control compounds dihydroartemisinin (DHA) and artemether, was dissolved in DMSO and spiked (500

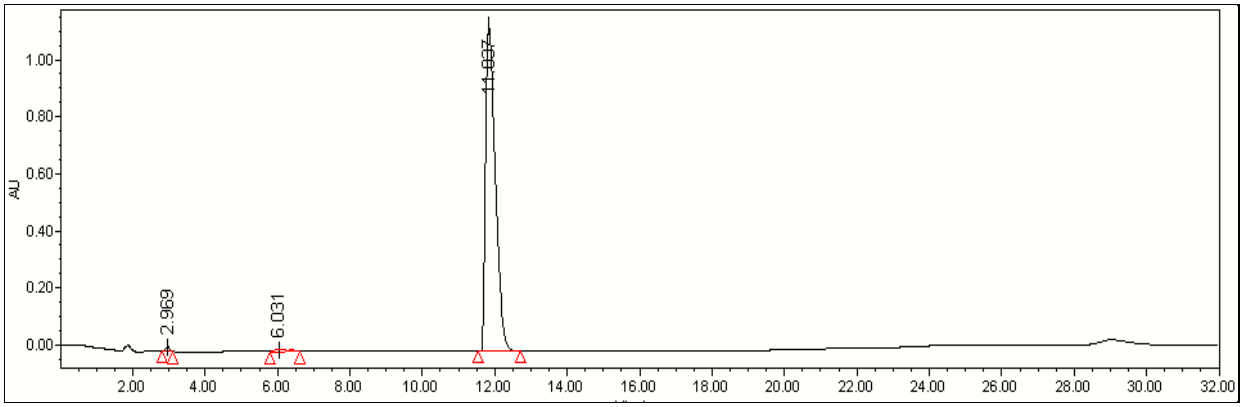
ng) into acetonitrile: 5mM ammonium acetate (1:1) and infused on the mass spectrometer, an AB Sciex API 5500 mass spectrometer operating at unit resolution in the multiple reaction monitoring (MRM) mode. At NWU, for the HPLC analyses, an Agilent 1100 series instrument equipped with a gradient pump, autosampler, diode array UV detector and OpenLab CDS Chemstation Rev.C.01.07 SR3 data acquisition and analysis software was used (Agilent Technologies, Palo Alto, CA, USA). The column was a Venusil XBP C18(2) -column, 150 x 4.6 mm, 5 µm spherical particles, 100 Å pore size (Agela Technologies, Newark, DE, USA). The mobile phase was acetonitrile and 0.1% orthophosphoric acid in water with a linear gradient from 30% acetonitrile to 85% after five minutes and holding until 15 minutes before equilibrating with 30% acetonitrile to 20 minutes. The flow rate was set at 1 mL/minute and the injection volume was 10 µL. The UV signal was monitored at 210 nm.

10-Amino artemisinins

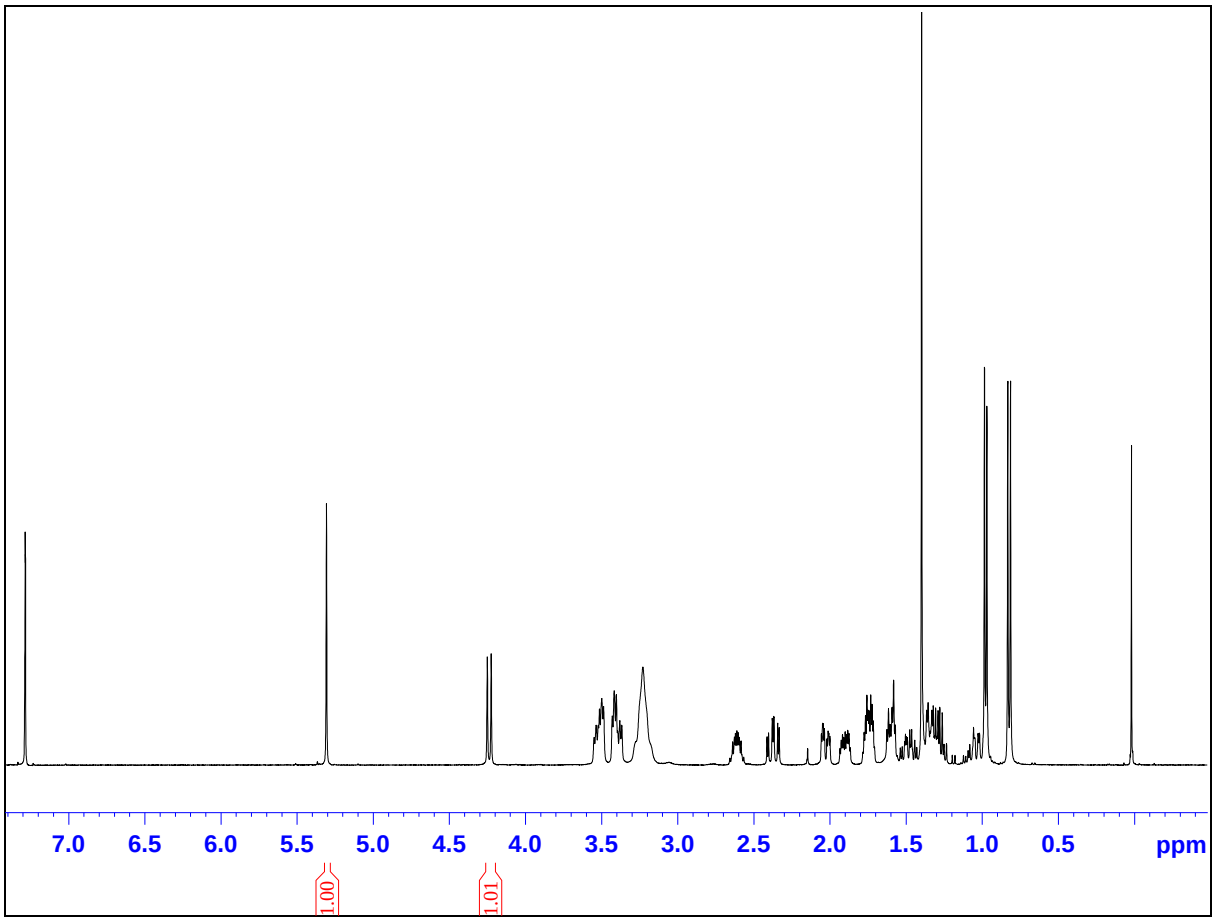
Artemisone: 1. MS (UCT): AB Sciex API 5500 spectrometer operating at unit resolution in multiple reaction monitoring and unit resolution modes; (M+H).

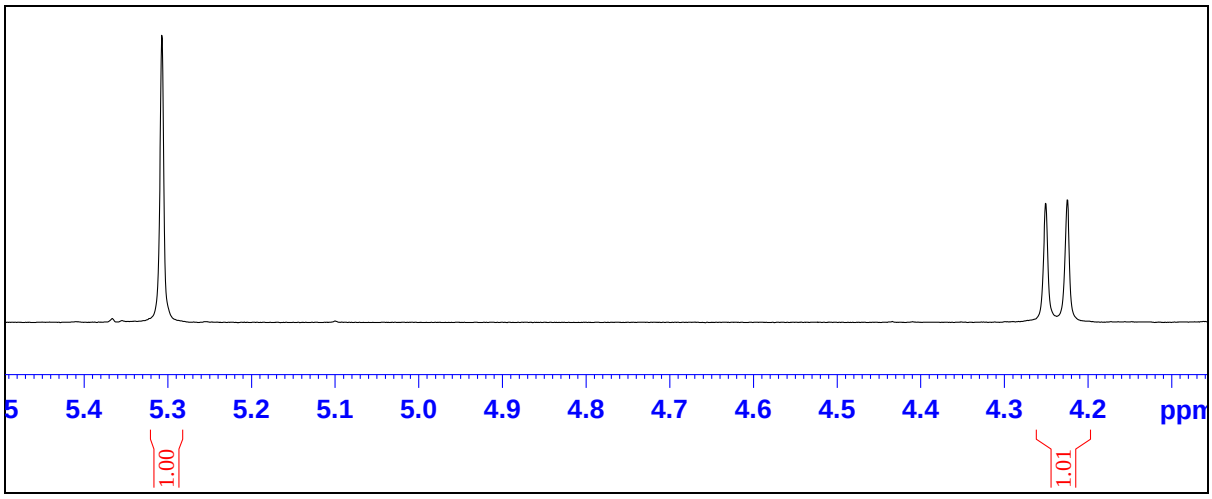


2. HPLC (HKUST): acetonitrile solution; YMC-Pack ODS-AQ 3 µm, 250 x 4.6 mm column; Waters 2996 Photodiode Array Detector, 600 Controller and TM 717 Plus Autosampler; data system Millennium32 Version 4.00; detection wavelength 195 nm; based on calibration with known impurities at 6.03 and 2.97 minutes, artemisone purity >98%.

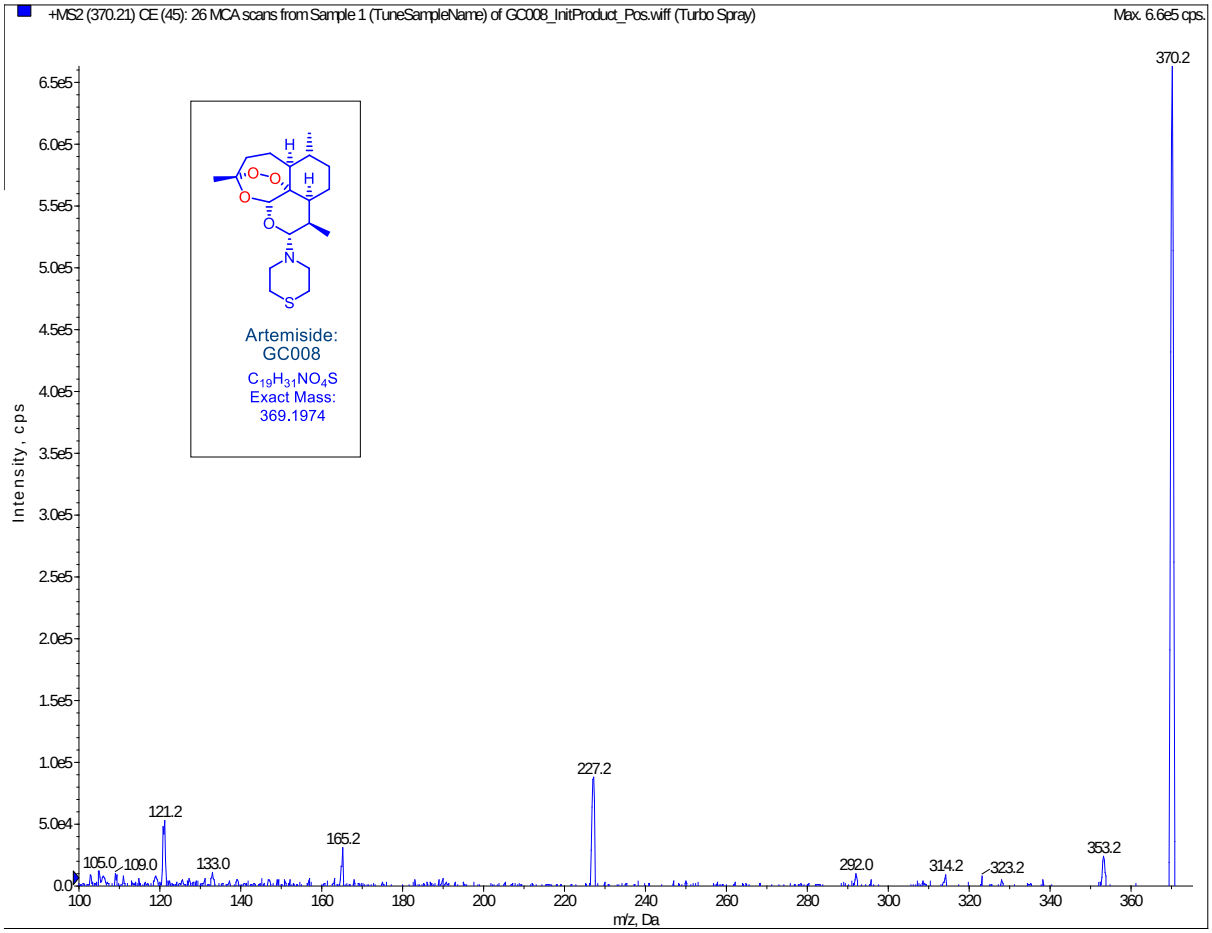


3. ^{1}H NMR ($CDCl_3$, 400 MHz) (HKUST):

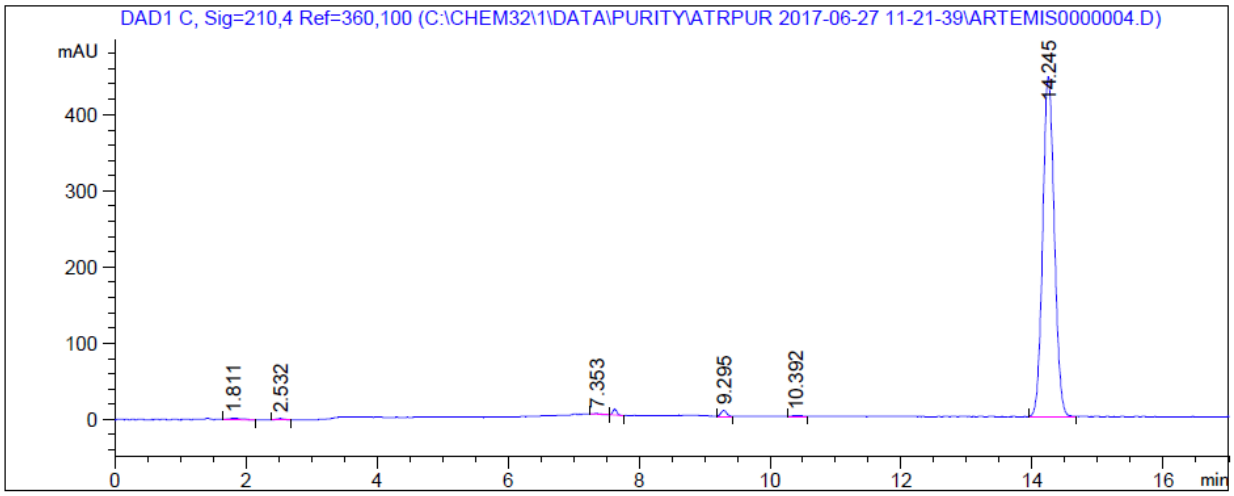




Artemiside: 1. MS (UCT): AB Sciex API 5500 spectrometer operating at unit resolution in multiple reaction monitoring and unit resolution modes; (M+H).



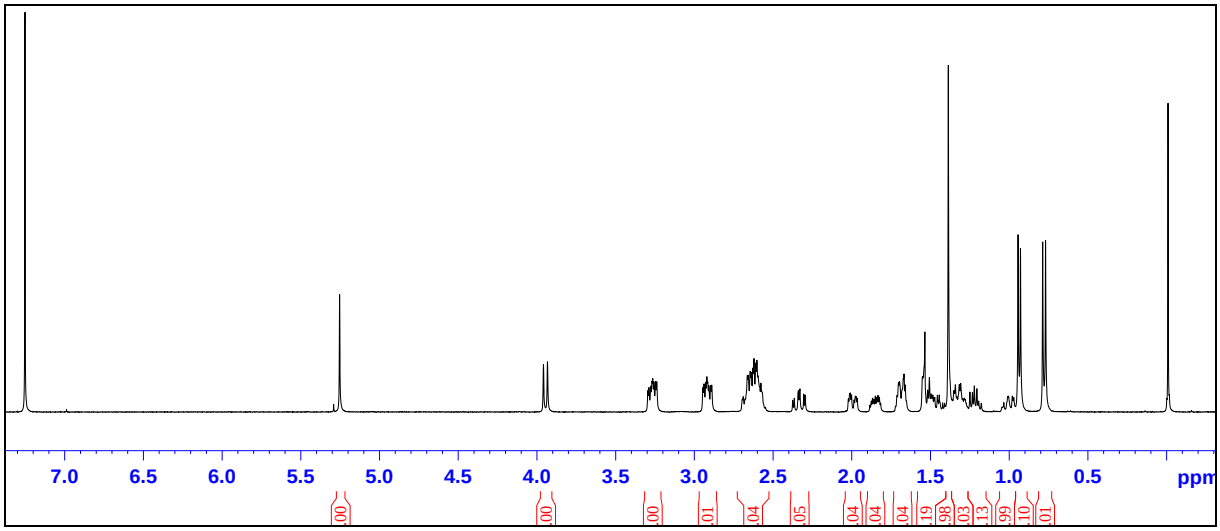
2. HPLC (NWU): see conditions above, artemiside purity >97%.

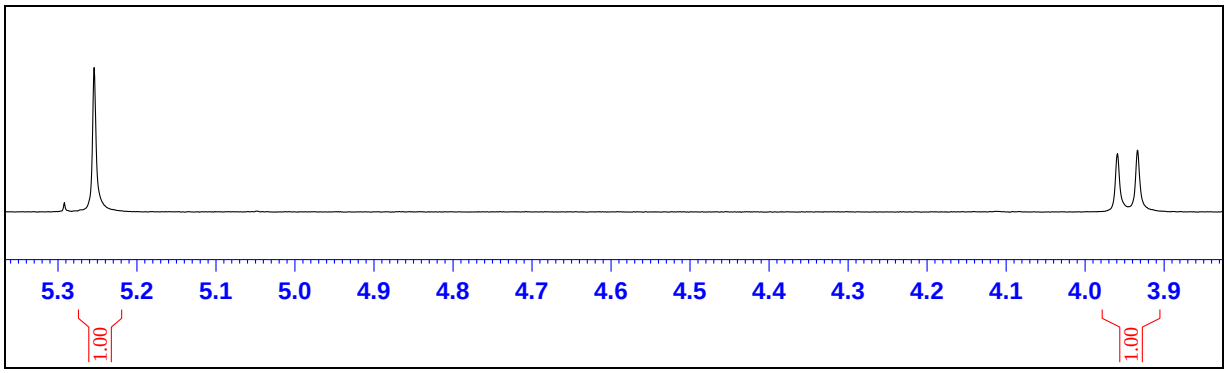


Artemiside HPLC analysis (cont.)

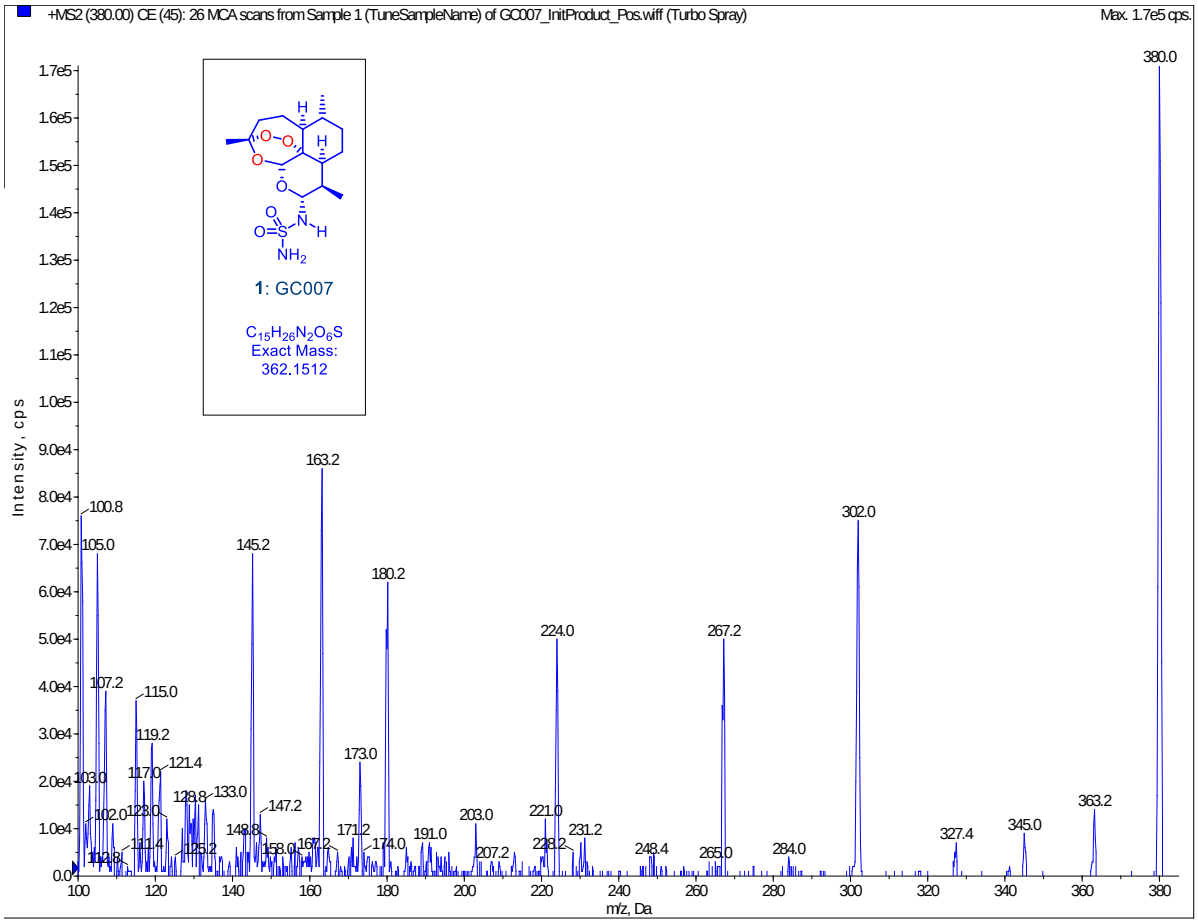
Peak #	RetTime [min]	Type	Width [min]	Area [mAU's]	Height [mAU]	Area %
1	1.811	BB	0.1810	31.34706	2.16365	0.5586
2	2.532	BB	0.0995	14.80692	2.06988	0.2639
3	7.353	BB	0.0849	6.11526	1.000634	0.1090
4	7.632	BB	0.0669	34.24465	7.85627	0.6102
5	9.295	BB	0.0894	44.91605	7.77421	0.8004
6	10.392	BB	0.0973	7.89385	1.10521	0.1407
7	14.245	BB	0.1901	5472.45117	446.34439	97.5173
Totals:				6511.77496	468.31994	

3. ^{1}H NMR ($CDCl_3$, 400 MHz) (HKUST):

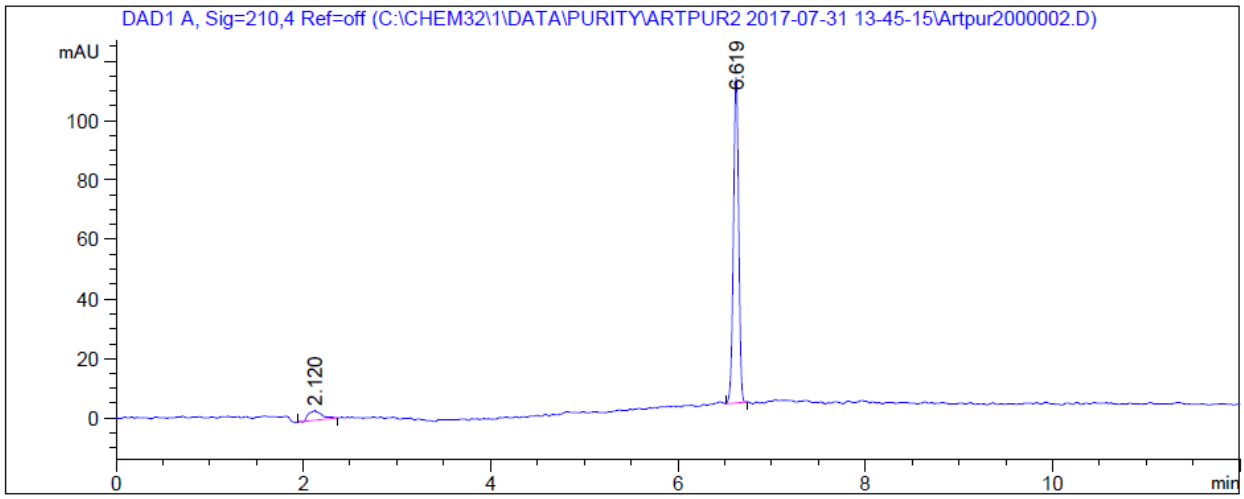




10-sulfamide compound 1. MS (UCT): AB Sciex API 5500 spectrometer operating at unit resolution in multiple reaction monitoring and unit resolution modes; ($M+NH_4$).



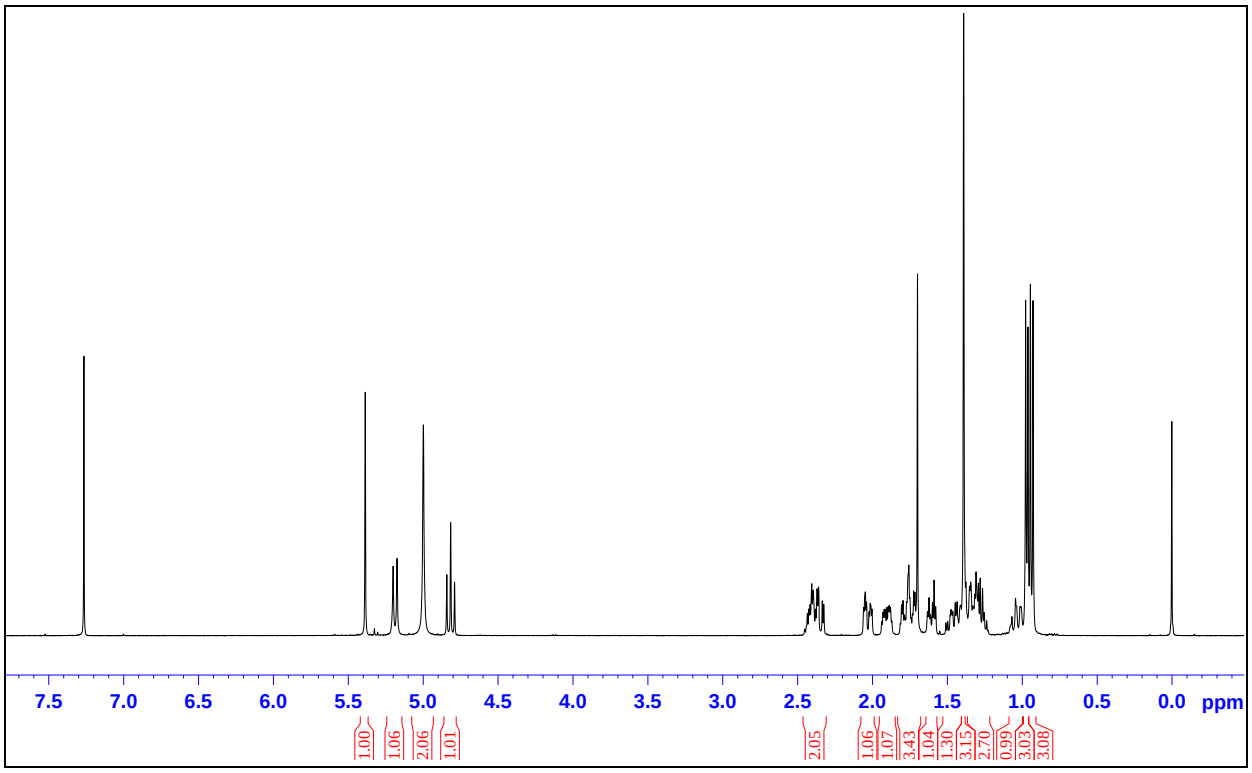
2. HPLC (NWU): see conditions above; 10-sulfamide purity 93%.

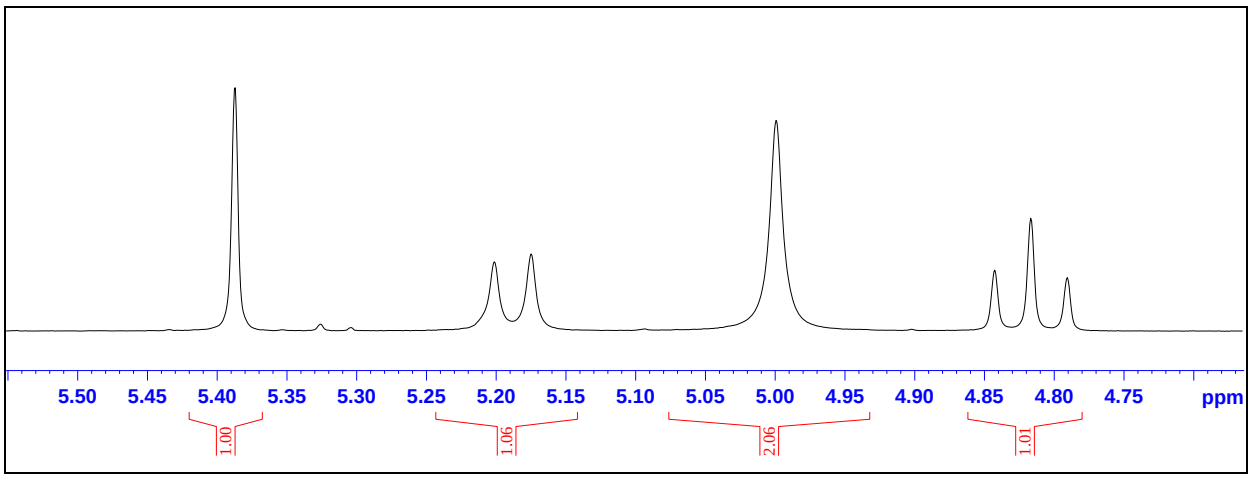


10-sulfamide continued: HPLC analysis (cont.)

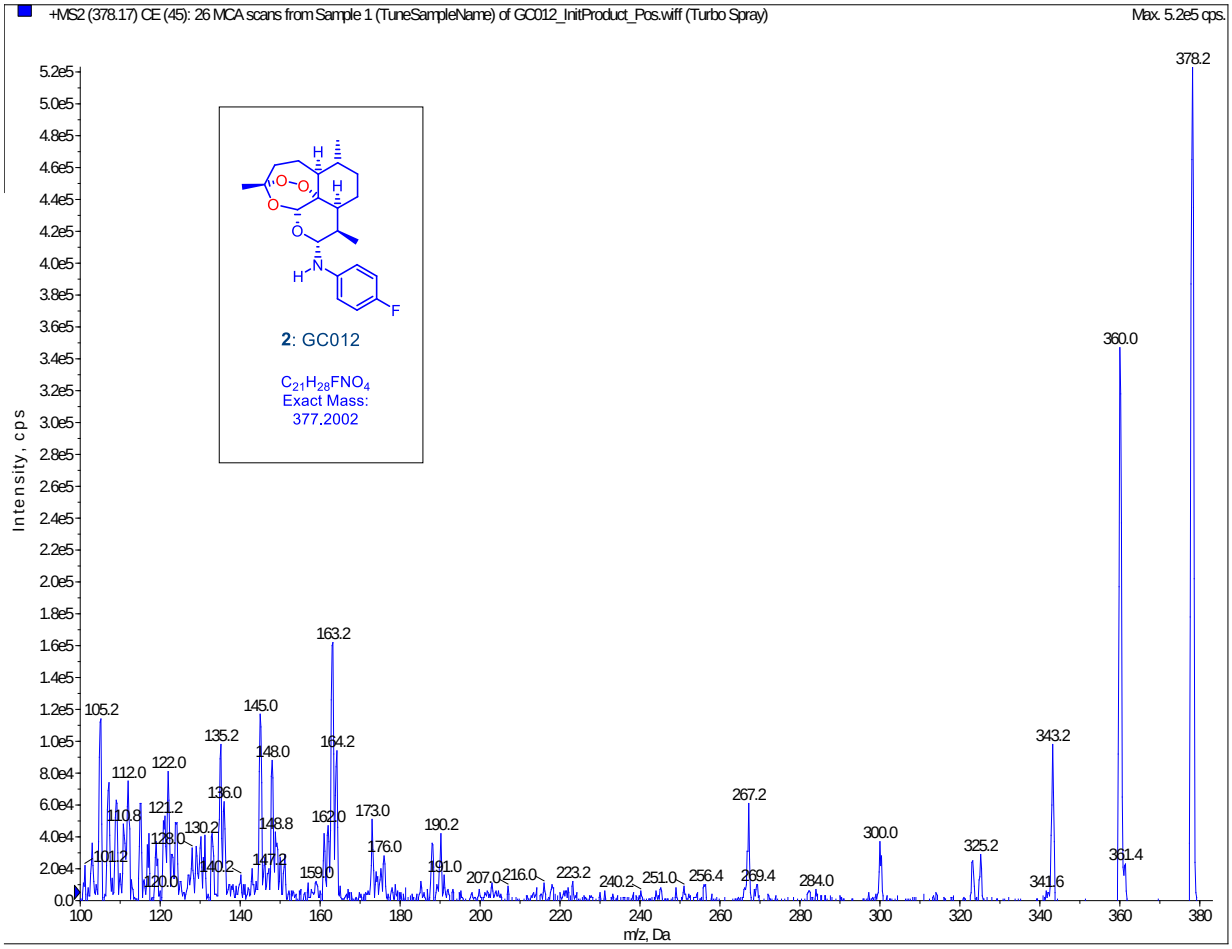
Peak #	RetTime [min]	Type	Width [min]	Area [mAU's]	Height [mAU]	Area %
1	2.120	BB	0.1343	31.76726	3.18671	6.8474
2	6.619	BB	0.0619	432.16391	109.75494	93.1526
Totals:				463.93117	112.94165	

3. ^{1}H NMR ($CDCl_3$, 400 MHz) (HKUST):

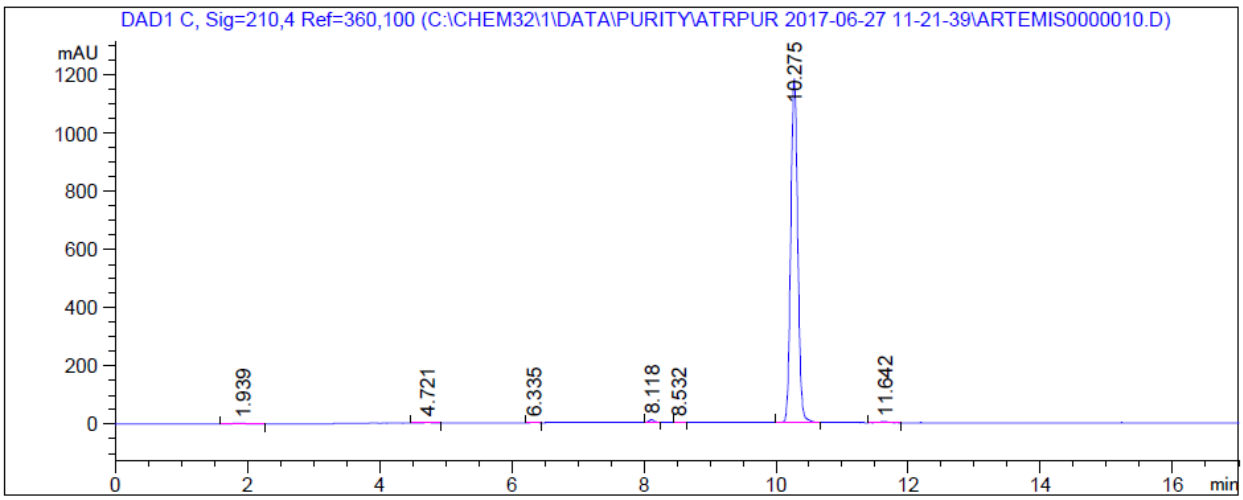




10-arylamine derivative 1. MS (UCT): AB Sciex API 5500 spectrometer operating at unit resolution in multiple reaction monitoring and unit resolution modes; (M+H).



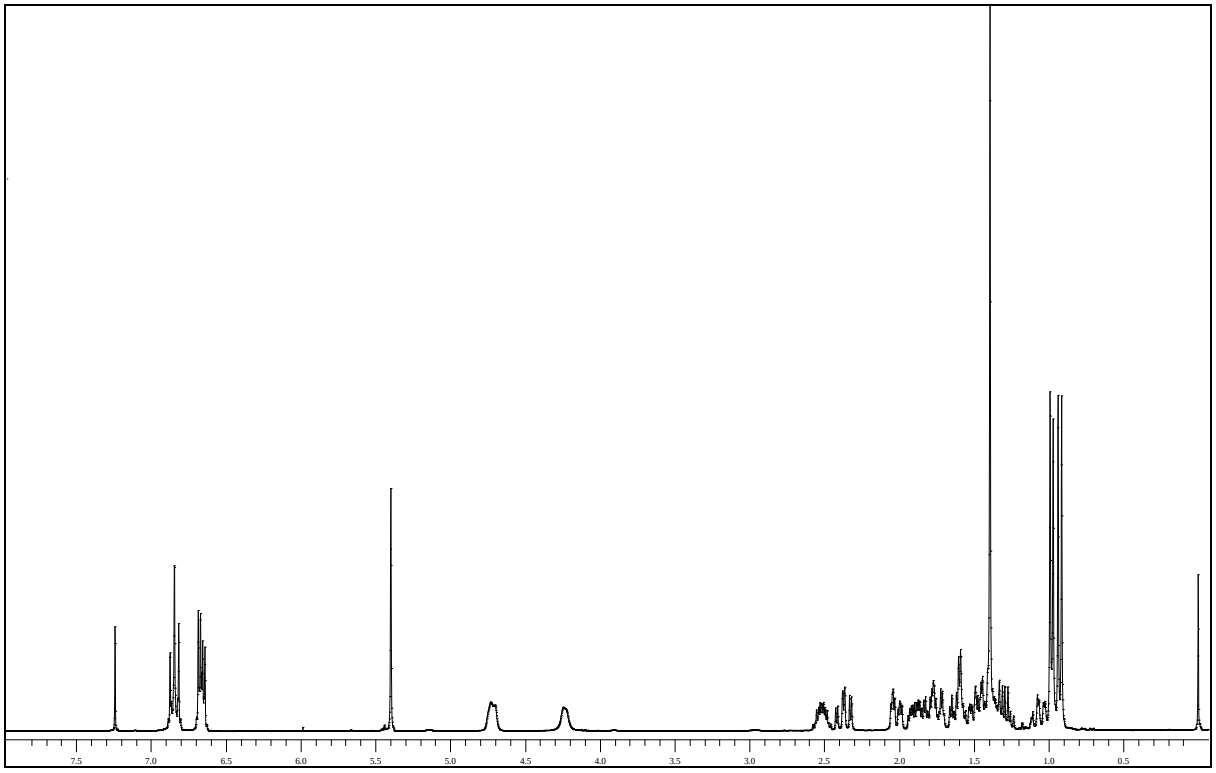
2. HPLC (NWU): see conditions above, 10-arylamine purity ≥98%.



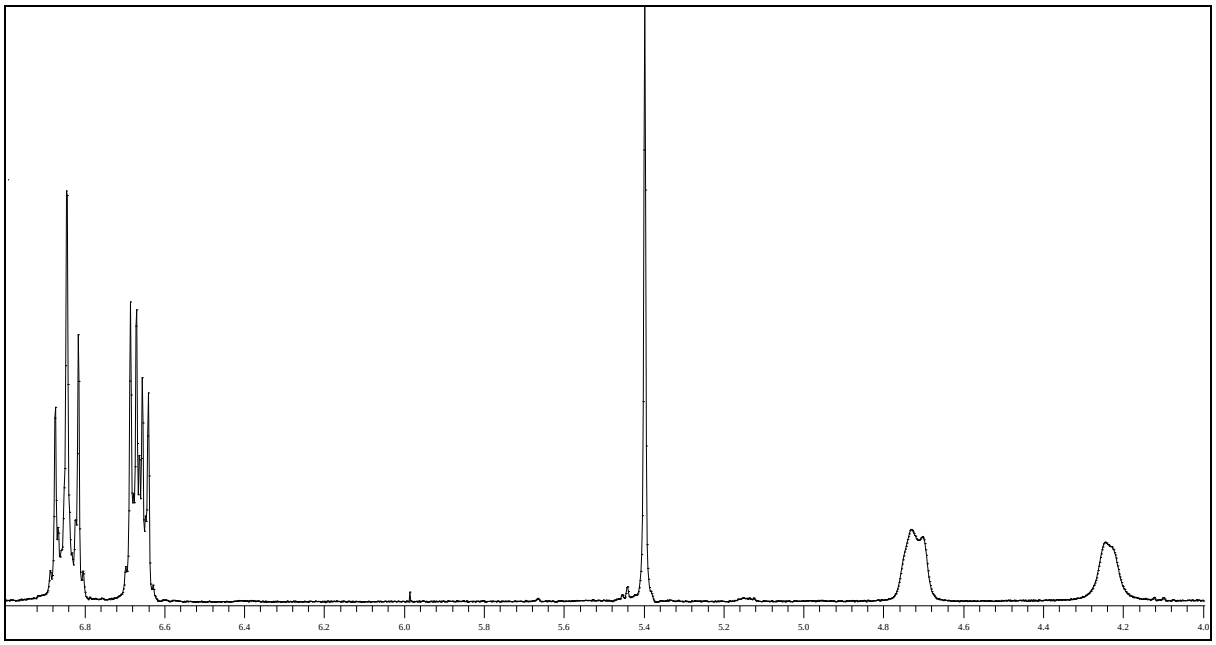
10-arylamine derivative HPLC analysis (cont.).

Peak #	RetTime [min]	Type	Width [min]	Area [mAU's]	Height [mAU]	Area %
1	1.939	BB	0.1802	18.99872	1.33357	0.2165
2	4.721	BB	0.0842	17.89655	3.15620	0.2039
3	6.335	BB	0.884	13.55796	2.18492	0.1545
4	8.118	BB	0.769	42.94182	8.50627	0.4893
5	8.53	BB	0.0870	5.84966	1.118817	0.0666
6	10.275	BB	0.1153	8648.04395	1182.75195	98.5336
7	11.624	BB	0.1311	29.46622	2.98582	0.3356
Totals:				8776.74498	1202.03690	

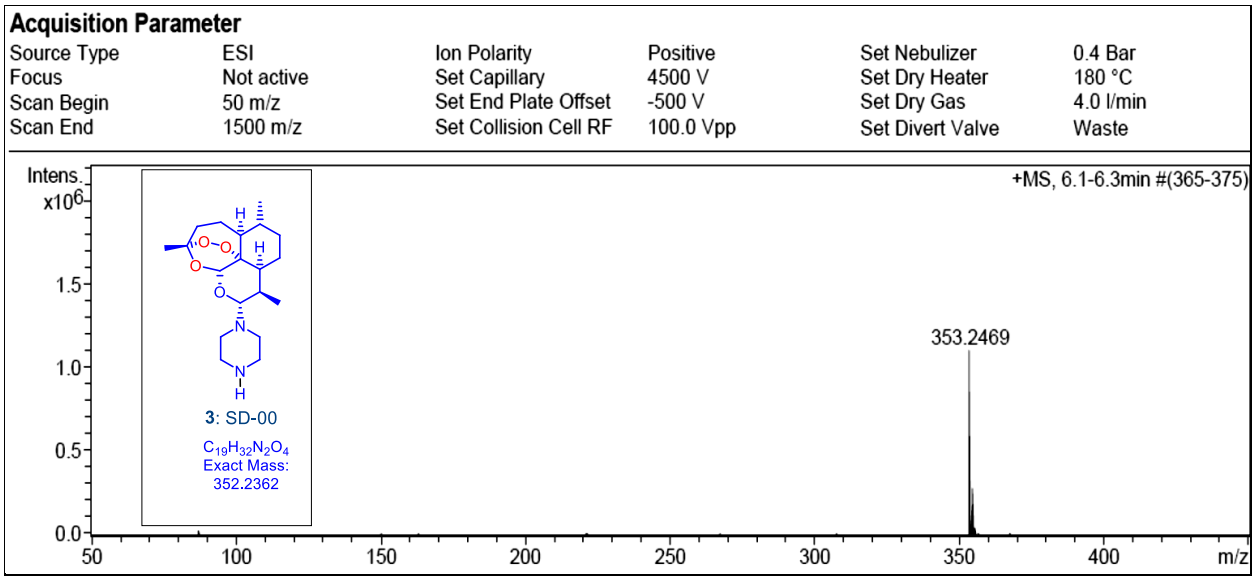
3. ^{1}H NMR ($CDCl_3$, 300 MHz) (HKUST):



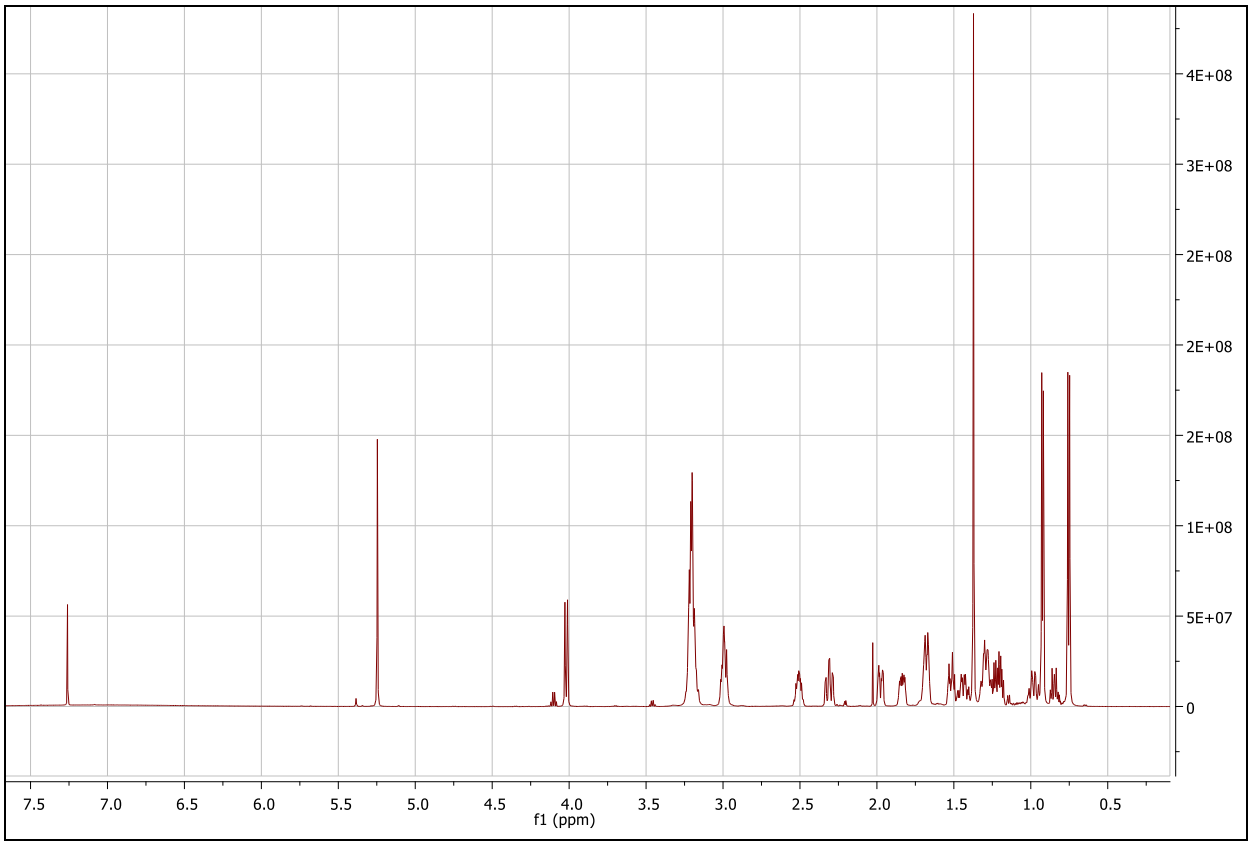
10-arylamine derivative NMR (cont.).

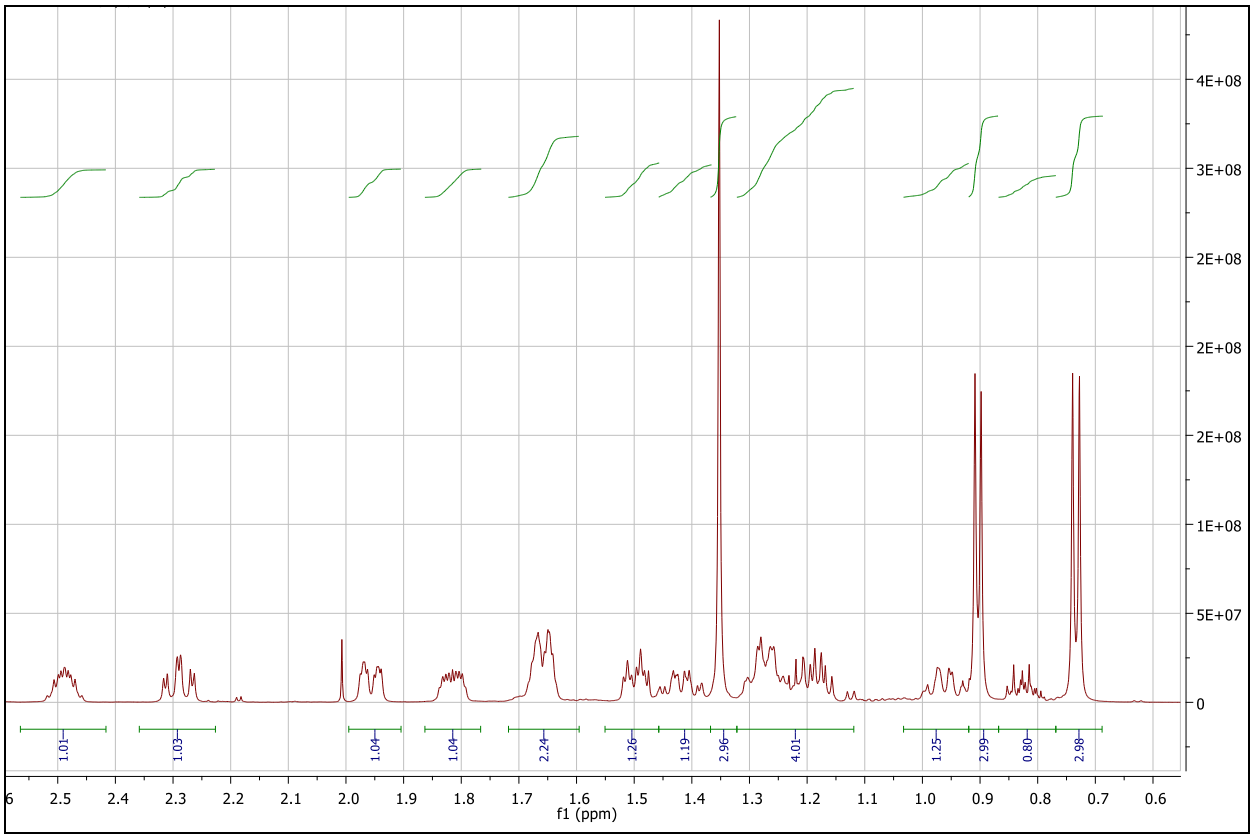


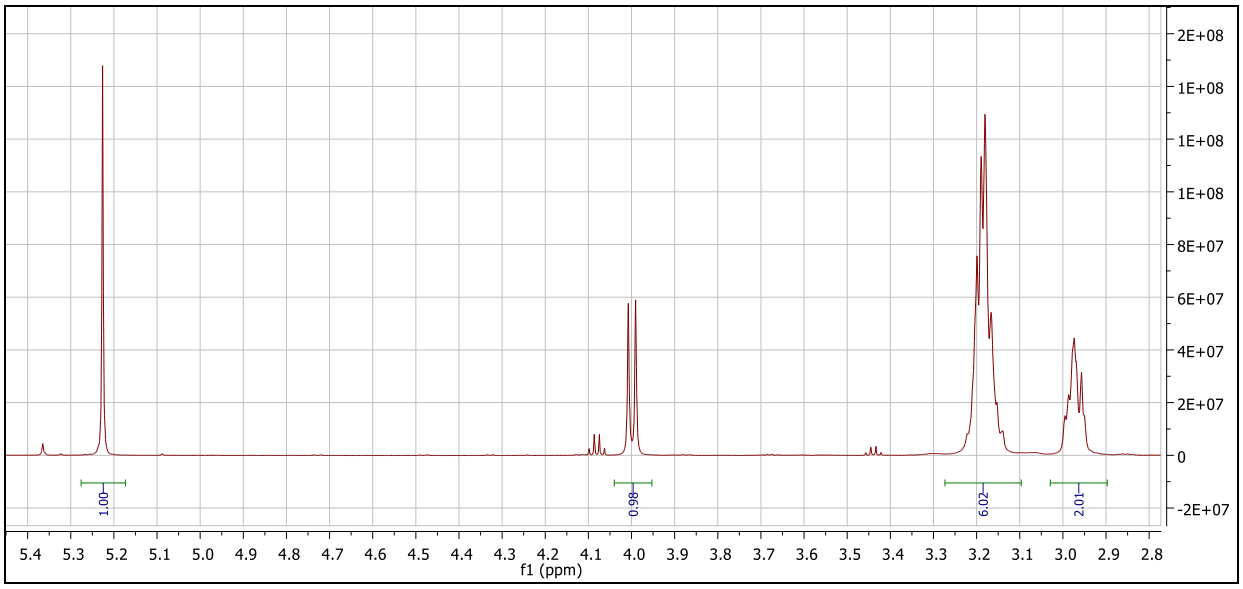
10-piperazine cderivative 1. MS (NWU): Bruker MicroTOF Q II mass spectrometer, ESI source (M + H), 10-piperazine derivative purity not determined.



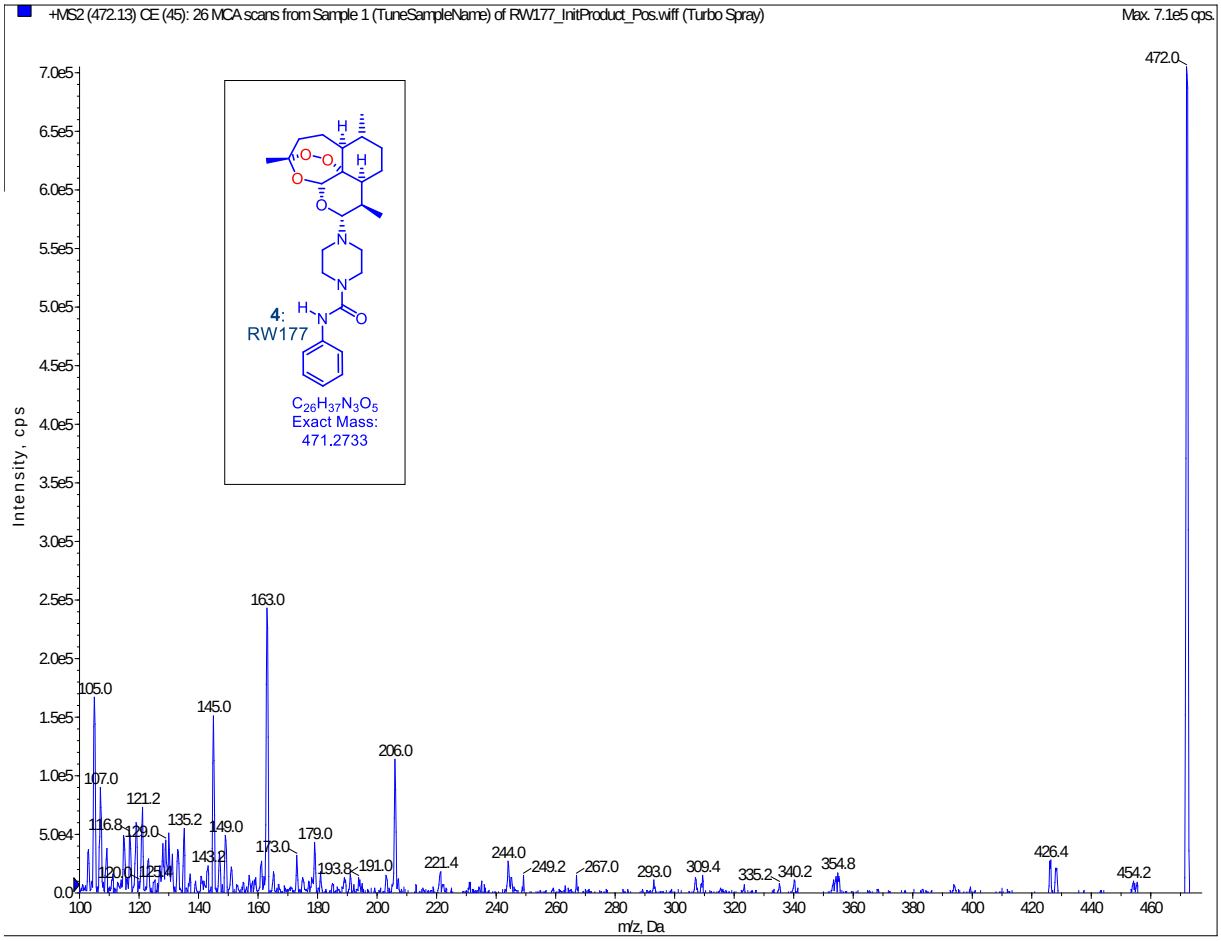
2. ^{1}HNMR spectrum ($CDCl_3$, 600 MHz) (NWU).



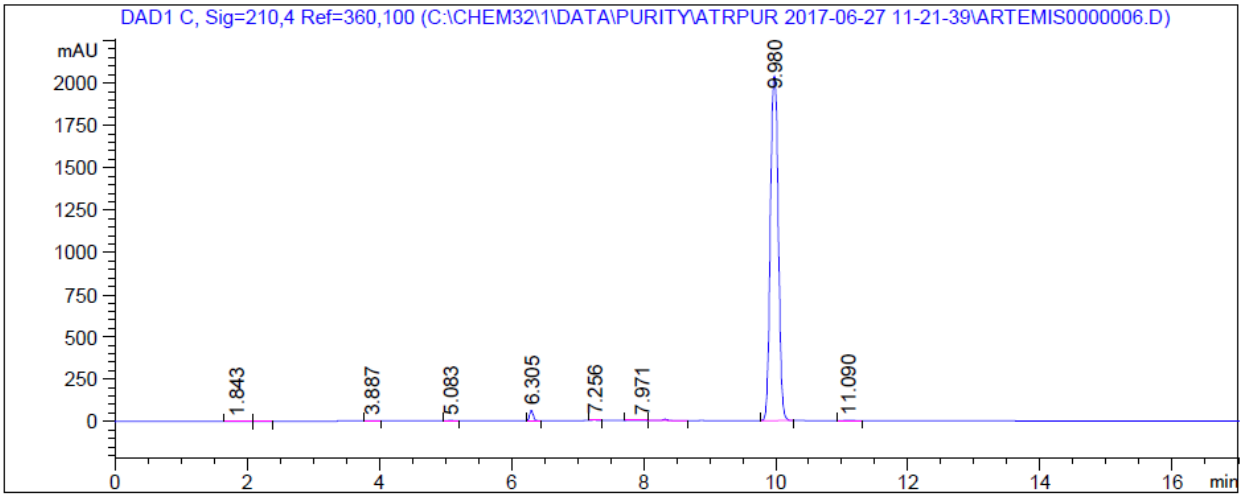

4E+08
3E+08
2E+08
2E+08
2E+08
2E+08
1E+08
5E+07
0
1.01
1.03
1.04
1.04
2.24
1.26
1.19
2.96
4.01
1.25
2.99
0.80
2.98
6 2.5 2.4 2.3 2.2 2.1 2.0 1.9 1.8 1.7 1.6 1.5 1.4 1.3 1.2 1.1 1.0 0.9 0.8 0.7 0.6
f1 (ppm)


2E+08
1E+08
1E+08
1E+08
8E+07
6E+07
4E+07
2E+07
0
-2E+07
1.00
0.98
6.02
2.01
5.4 5.3 5.2 5.1 5.0 4.9 4.8 4.7 4.6 4.5 4.4 4.3 4.2 4.1 4.0 3.9 3.8 3.7 3.6 3.5 3.4 3.3 3.2 3.1 3.0 2.9 2.8
f1 (ppm)

10-phenylurea derivative 1. MS (UCT): AB Sciex API 5500 spectrometer operating at unit resolution in multiple reaction monitoring and unit resolution modes; (M+H).

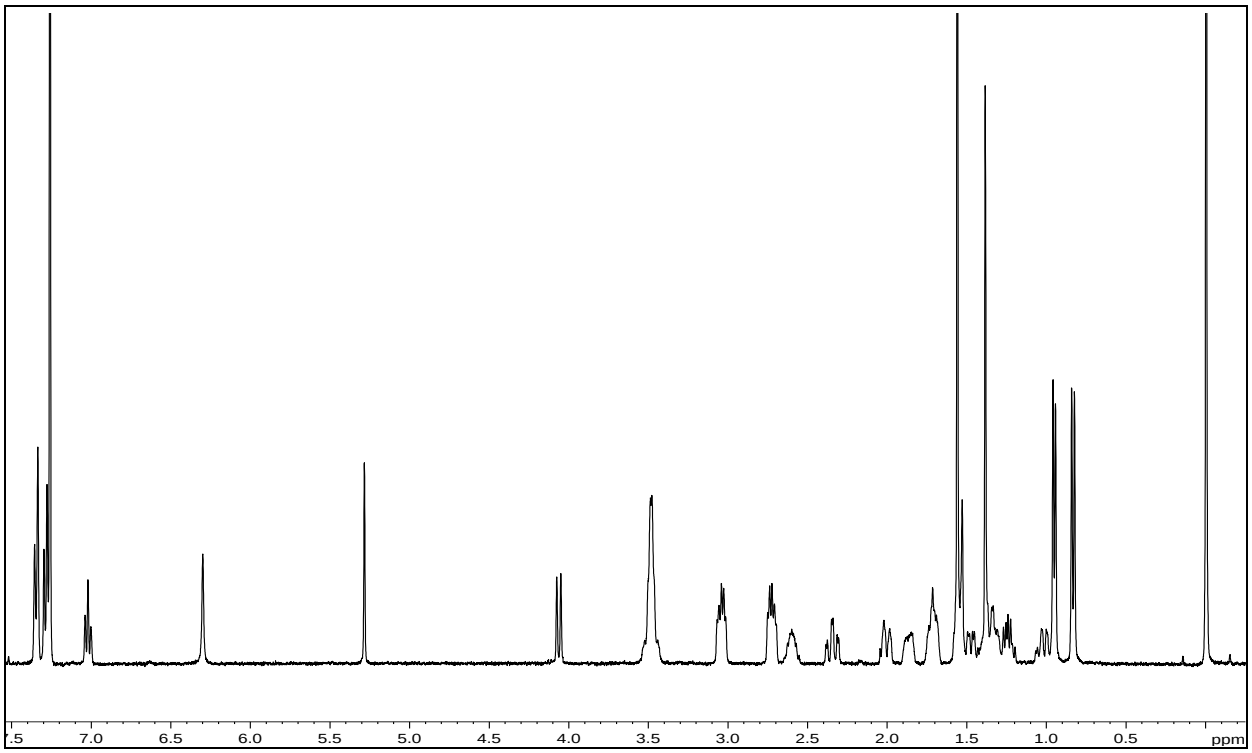


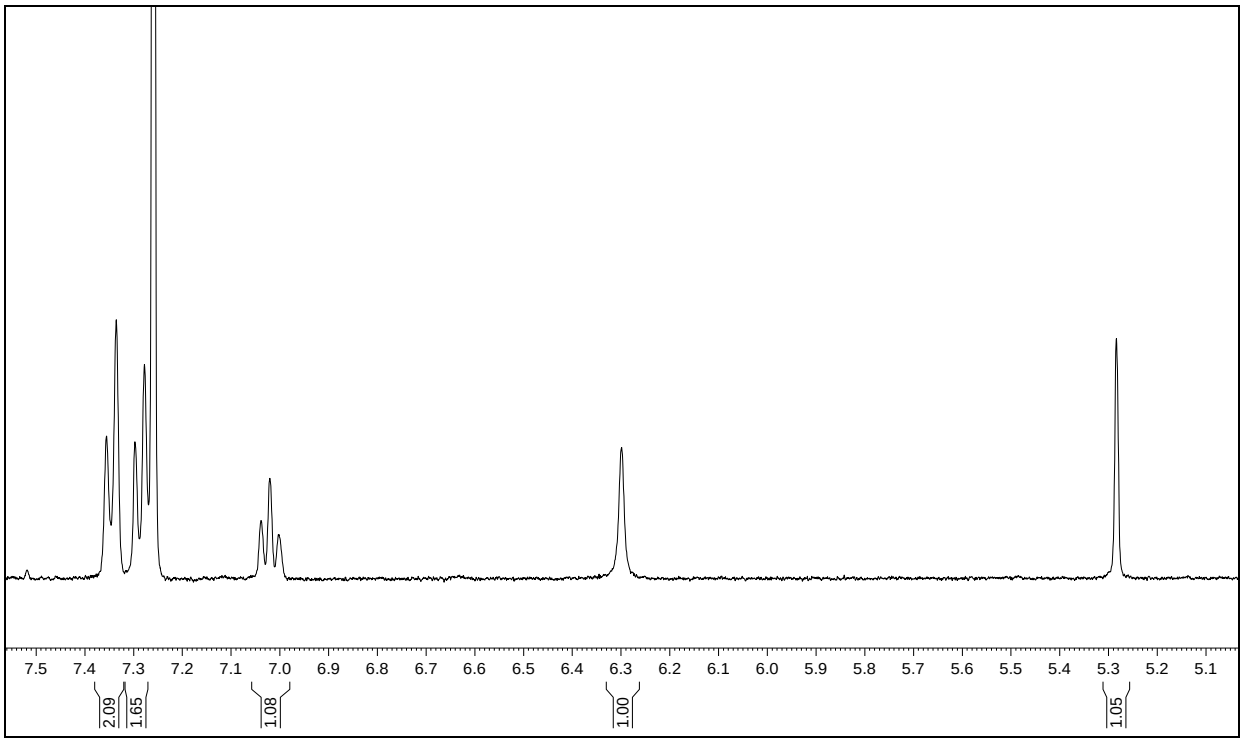
2. HPLC (NWU): see conditions above, compound 10-phenylurea derivative purity ≥98%.



Peak #	RetTime [min]	Type	Width [min]	Area [mAU's]	Height [mAU]	Area %
1	1.843	BB	0.1701	19.38464	1.43061	0.1118
2	2.181	BB	0.1307	15.62486	1.48608	0.0901
3	3.887	BB	0.0970	18.64808	2.75565	0.1076
4	5.083	BB	0.0673	23.65286	5.37699	0.1364
5	6.305	BB	0.0609	232.72781	60.48832	1.3425
6	7.256	BB	0.0666	22.32742	5.14747	0.1288
7	7.971	BB	0.1127	10.60549	1.20498	0.0612
8	8.327	BB	0.0856	43.55238	7.51311	0.2512
9	9.980	BB	0.1330	1.69370e4	2037.33716	97.7028
10	11.090	BB	0.1111	11.70701	1.40589	0.0675

3. ^{1}H NMR spectrum (400 MHz) (HKUST):




7.5 7.4 7.3 7.2 7.1 7.0 6.9 6.8 6.7 6.6 6.5 6.4 6.3 6.2 6.1 6.0 5.9 5.8 5.7 5.6 5.5 5.4 5.3 5.2 5.1
2.09
1.65
1.08
1.00
1.05

Part 2 Biology

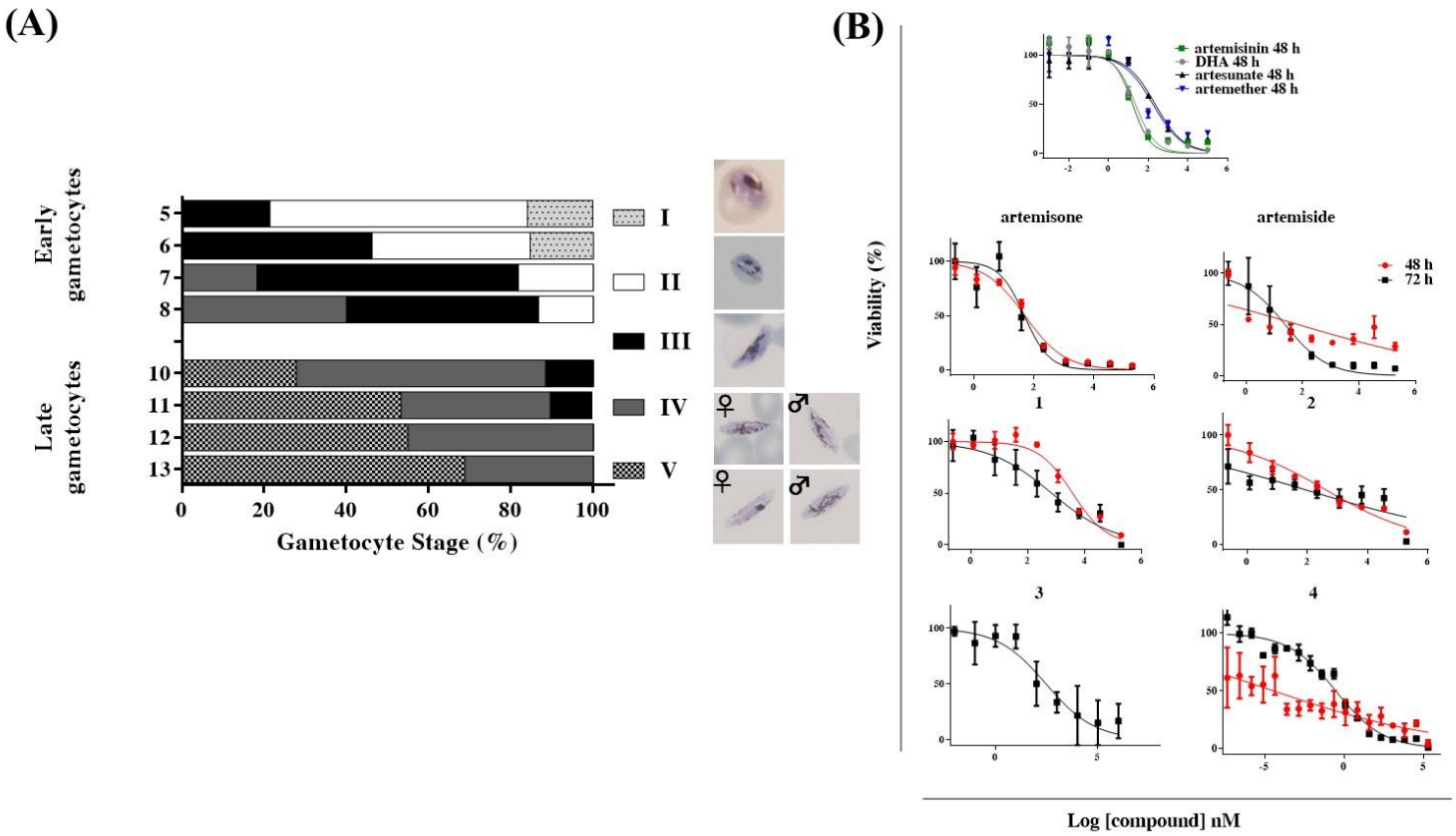


Figure S1: (A) Early and late stage gametocyte assay metrics. Gametocyte stage confirmation and percentage using Giemsa smears over the assay time periods. Assays for early stage gametocytes were performed on day 5 cultures (~100% stage I-III) and day 10 for late stage gametocytes (~90% late stage IV/V). **(B)** Gametocytocidal kill kinetics of oxidant compounds against late stage gametocytes. Sigmoidal dose-response curves were obtained for the precursor compounds at 48 h for late stage gametocytes with the luciferase assay. Data are the mean ±SEM from three independent experiments performed in triplicate. Dose-response curves for 48 h (black curve) and 72 h (red curve) for the 10-alkylaminoartemisinins for late stage gametocytes performed with the luciferase assay. Data are means of two or three biological repeats (n=2/3) performed in technical triplicates, error bars indicate ±SEM for n=3

and ±SD for n=2.

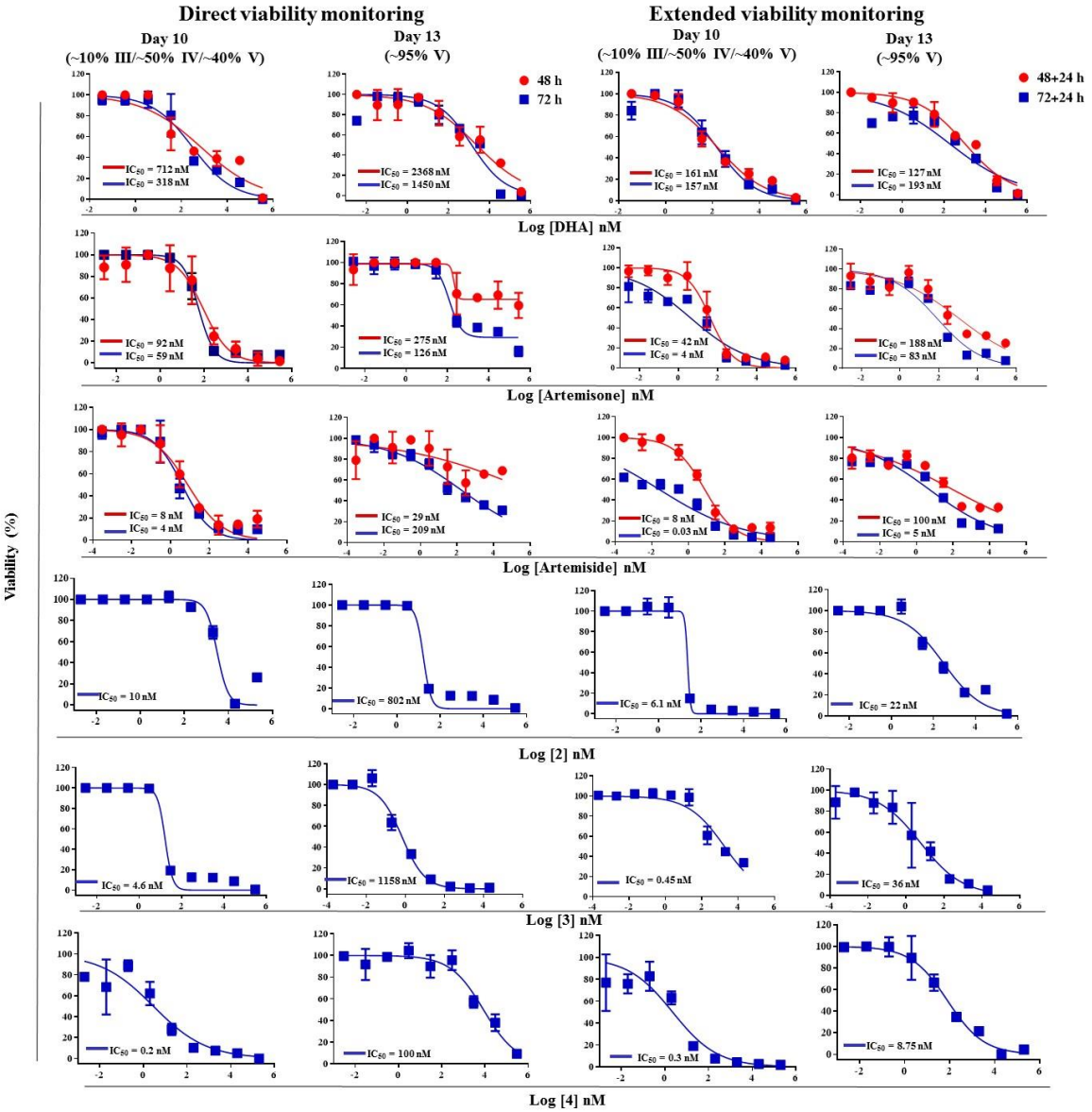


Figure S2: Stage specificity, speed-of-action and transmission blocking-gametocytocidal action of DHA, artemisone, artemiside, 10-arylamine, 10-piperazine, and 10-phenylurea against stage IV/V and stage V gametocyte populations. Activities of reference compound, DHA, with late stage specific compounds artemisone, artemiside, 10-arylamine, 10-piperazine, and 10-phenylurea against stage IV and V gametocytes. Full dose-response gametocyte

viability was measured over time at 48 and 72 h (DHA, artemisone and artemiside) and 72 h (10-arylamine, 10-piperazine, and 10-phenylurea) using the luciferase assay. In addition, gametocyte viability was measured over time at 48, and 72 h including an extended 24 h incubation without the presence of drug. In all instances are data from one biological repeat, performed in technical triplicates, ±SD indicated.