Electronic Supplementary Material (ESI) for RSC Medicinal Chemistry. This journal is © The Royal Society of Chemistry 2022

Supplementary Material

¹H, ¹³C NMR, & HRMS Spectra of Representative Compounds

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Spectras of representative compounds

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Single Mass Analysis Tolerance = 300.0 PPM / DBE: min = -1.5, max = 50.0 Element prediction: Off Number of isotope peaks used for i-FIT = 5

Monoisotopic Mass, Even Electron Ions 5 formula(e) evaluated with 1 results within limits (all results (up to 1000) for each mass) Elements Used: C: 18-18 H: 0-300 N: 0-4 O: 1-1 Sample Name : 280921_AK-1 Test Name : 280921_AK-1 20 (0.435) IITRPR XEVO G2-XS QTOF 1: TOF MS ES+ 2.47e+007 292.1458 100-%-293.1492







Figure 1. Spectras of compound AK-1

Single Mass Analysis Tolerance = 300.0 PPM / DBE: min = -1.5, max = 50.0 Element prediction: Off Number of isotope peaks used for i-FIT = 5

Monoisotopic Mass, Even Electron Ions 10 formula(e) evaluated with 1 results within limits (all results (up to 1000) for each mass) Elements Used: C: 19-19 H: 0-300 N: 0-4 O: 1-1 S: 0-1 Sample Name : 280921_AK-2 IITRPR XEVO G2-XS QTOF Test Name 280921_AK-2 21 (0.452) 1: TOF MS ES+ 2.52e+007 338 1333

100				330	.1335							
%	137.0027	217.0	159	323.1102	339.1362 _340.1332 44	41.3047	537.5377		663.4565 74	1.4718 777.303	3_833.4727	960.5997 m/z
10	0	200		300	400		500	600	700	800	900	1000
Minim Maxim	um: um:			2.0	300.0	-1.5 50.0						
Mass		Calc.	Mass	mDa	PPM	DBE	i-FIT	Norm	Conf(%)	Formula		
338.1	333	338.13	327	0.6	1.8	11.5	1621.8	n/a	n/a	C19 H20 N	3 O S	





Figure 2. Spectras of compound AK-2

Single Mass Analysis Tolerance = 300.0 PPM / DBE: min = -1.5, max = 50.0 Element prediction: Off Number of isotope peaks used for i-FIT = 5

Monoisotopic Mass, Even Electron Ions 5 formula(e) evaluated with 0 results within limits (all results (up to 1000) for each mass) Elements Used: C: 18-18 H: 0-300 N: 0-4 O: 1-1 F: 6-6

Sample Name : 280921_AK-3 Test Name 280921_AK-3 23 (0.497)

IITRPR





XEVO G2-XS QTOF



Figure 3. Spectras of compound AK-3

Single Mass Analysis

Tolerance = 300.0 PPM / DBE: min = -1.5, max = 50.0 Element prediction: Off Number of isotope peaks used for i-FIT = 5





11.0 10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 -0.5 fi (ppm)



Figure 4. Spectras of compound AK-4

Single Mass Analysis

Tolerance = 300.0 PPM / DBE: min = -1.5, max = 50.0 Element prediction: Off Number of isotope peaks used for i-FIT = 5

Monoisotopic Mass, Even Electron Ions 10 formula(e) evaluated with 1 results within limits (all results (up to 1000) for each mass) Elements Used: C: 18-18 H: 0-300 N: 0-4 O: 1-2 Sample Name : 280921_AK-5 IITRPR XEVO G2-XS QTOF Test Name 280921_AK-5 34 (0.729) 1: TOF MS ES+ 3.38e+006 308.1405 100 %-309.1436 137.0028 217.0161 663.4575 745.4238 833.4746 970.5886 m/z 1000 310.1456 441.3015 537.5375,565.5680 0 200 700 800 100 300 400 500 600 900 -1.5 Minimum: Maximum: 2.0 300.0 50.0 DBE Conf(%) Formula Mass Calc. Mass mDa PPM i-FIT Norm 308.1405 308.1399 0.6 1.9 11.5 1936.7 n/a n/a C18 H18 N3 O2



9.4 9.2 9.0 8.8 8.6 8.4 8.2 8.0 7.8 7.6 7.4 7.2 7.0 6.8 6.6 6.4 6.2 6.0 5.8 5.6 5.4 5.2 5.0 4.8 4.6 4.4 4.2 4.0 3.8 3.6 3.4 f1 (ppm)

Figure 5. Spectras of compound AK-5





Figure 6. Spectras of compound AK-6

Single Mass Analysis Tolerance = 300.0 PPM / DBE: min = -1.5, max = 50.0 Element prediction: Off Number of isotope peaks used for i-FIT = 5

Monoisotopic Mass, Even Electron Ions 25 formula(e) evaluated with 1 results within limits (all results (up to 1000) for each mass) Elements Used: C: 21-21 H: 0-300 N: 0-4 O: 0-4 Sample Name : 280921_AK-7 IITRPR Test Name : 280921_AK-7 27 (0.576)

100					382.	1770											1.1	
%- 137.00	29	217.0	159	274.2757		383.11 384.	804 1841	53	7.5372	.565.569	6663.45	574	745.4251	789.	4498		960.5993	m/z
100 1	50	200	250	300	350	400	450	500	550	600	650	700	750	800	850	900	950	1 1192
Minimum: Maximum:				2.0	300	0.0	-1.5 50.0											
Mass	Ca	lc.	Mass	mDa	PPI	м	DBE	i-1	FIT	Norm	Co	nf(%) Form	nula				
382.1770	38	2.17	767	0.3	0.0	в	11.5	14	20.1	n/a	n/	a	C21	H24	N3 04			



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XEVO G2-XS QTOF

1: TOF MS ES+ 7.28e+006



Figure 7. Spectras of compound AK-7

Single Mass Analysis Tolerance = 300.0 PPM / DBE: min = -1.5, max = 50.0 Element prediction: Off Number of isotope peaks used for i-FIT = 5 Monoisotopic Mass, Even Electron Ions 15 formula(e) evaluated with 1 results within limits (all results (up to 1000) for each mass) Elements Used: C: 19-19 H: 0-300 N: 0-4 O: 0-2 Sample Name : 280921_AK-8 IITRPR Test Name : 280921_AK-8 29 (0.622) 322.1561 100 %-323.1592 537.5371_565.5698663.4578 701.3993 701.3993 789.4498 877.4985 984.6078 217.0159 137.0028 324.1628 448.0549 0-htp:/// min minimum TTT IT minutum in the second s . . 111111 350 450 550 650 100 150 200 250 300 400 500 600 700 750 800 850

Minimum: Maximum:		2.0	300.0	-1.5 50.0				
Mass	Calc. Mass	mDa	PPM	DBE	i-FIT	Norm	Conf(%)	Formula
322.1561	322.1556	0.5	1.6	11.5	1507.9	n/a	n/a	C19 H20 N3 O2



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XEVO G2-XS QTOF

950

900

1: TOF MS ES+ 1.30e+007



Figure 8. Spectras of compound AK-8





Figure 9. Spectras of compound AK-9

Single Mass Analysis

Tolerance = 300.0 PPM / DBE: min = -1.5, max = 50.0 Element prediction: Off Number of isotope peaks used for i-FIT = 5

Monoisotopic Mass, Even Electron Ions 21 formula(e) evaluated with 6 results within limits (all results (up to 1000) for each mass) Elements Used: C: 20-21 H: 0-300 N: 0-4 O: 0-2 Sample Name : 280921_AK-10 IITRPR XEVO G2-XS QTOF Test Name : 280921_AK-10 20 (0.435) 1: TOF MS ES+ 1.48e+007 308.1409 100-% 309.1440 872.5430 970.5920 m/z 217.0161 266.1304 789.4512 310.1476 6 441.3020 537.5374,565.5696663.4573 741.4725 0 ntpromanh 11111 450 100 150 200 250 300 350 400 500 550 600 650 700 750 800 850 900 950

Minimum: Maximum:		2.0	300.0	-1.5				
Mass	Calc. Mass	mDa	PPM	DBE	i-FIT	Norm	Conf(%)	Formula
308.1409	308.1188 308.1651 308.0824 308.2014 308.0712	22.1 -24.2 58.5 -60.5 69.7	71.7 -78.5 189.8 -196.3 226.2	16.5 10.5 17.5 9.5 17.5	1567.9 1566.7 1566.7 1567.6 1568.1	2.578 1.401 1.427 2.309 2.829	7.60 24.65 24.00 9.94 5.91	C21 H14 N3 C20 H22 N O2 C20 H10 N3 O C21 H26 N O C21 H10 N O2





Figure 10. Spectras of compound AK-10

Single Mass Analysis

Tolerance = 300.0 PPM / DBE: min = -1.5, max = 50.0 Element prediction: Off Number of isotope peaks used for i-FIT = 5

Monoisotopic Mass, Even Electron Ions 40 formula(e) evaluated with 1 results within limits (all results (up to 1000) for each mass) Elements Used: C: 18-18 H: 0-300 N: 0-4 O: 0-1 CI: 0-1 F: 0-1

Sample Name : 280921_AK-11 Test Name : 280921_AK-11 22 (0.480) XEVO G2-XS QTOF 1: TOF MS ES+ 1.33e+007



IITRPR





Figure 11. Spectras of compound AK-11

Single Mass Analysis

Tolerance = 300.0 PPM / DBE: min = -1.5, max = 50.0 Element prediction: Off Number of isotope peaks used for i-FIT = 5

Monoisotopic Mass, Even Electron lons 10 formula(e) evaluated with 1 results within limits (all results (up to 1000) for each mass) Elements Used: C: 19-19 H: 0-300 N: 0-4 O: 0-1 Sample Name : 280921_AK-12 IITRPR XEVO G2-XS QTOF Test Name 280921_AK-12 22 (0.480) 1: TOF MS ES+ 5.97e+006 306.1614 100 %-307.1645 432.0577 ----704 0000 700 4540

0 137.00	28 217.0	158	30	08.1676	1	517.1537	505.5082	663.4567 /01.	3983 78	9.4510	903.191	8 968.6106	m/z
100 1	50 200	250	300	350 400	450	500 550	600	650 700	750 80	0 850	900	950	
Minimum: Maximum:			2.0	300.0	-1.5 50.0								
Mass	Calc.	Mass	mDa	PPM	DBE	i-FIT	Norm	Conf(%)	Formula				
306.1614	306.1	606	0.8	2.6	11.5	1385.2	n/a	n/a	C19 H20	N3 0			





Figure 12. Spectras of compound AK-12

Single Mas	ss Anal	ysis									
Tolerance =	300.0 P	PM /	DBE: r	nin = -1.5	, max =	= 50.0					
Element pre	diction:	Off									
Number of is	sotope p	eaks u	sed for i	-FIT = 5							
Monoisotopic 32 formula(e) Elements Use	Mass, E evaluate	ven Ele	ctron Ion 1 results	s within limit	s (all re	sults (up to 1	000) for	each mass)			
C: 19-19 H:	0-300	N: 0-3	O: 0-1	F: 0-3							
Sample Name	: 28092	1_AK-13				IITRPR				XEV	G2-XS QTOF
280921_AK-13	15 (0.328)									1	: TOF MS ES+ 2.35e+007
100			36	0.1330							
[%]				361.1364							
2	17.0159 2	91.0758	318.1227	362 1397	486	0303 548 1784	4	663 4553 74	1 4695 784.495	1872 5463	980 5728
0 -1	200	250	300 3	50 400	450	500 550	600	650 700	750 800	850 900	950
Minimum:					-1.5						
Maximum:			2.0	300.0	50.0						
Mass	Calc.	Mass	mDa	PPM	DBE	i-FIT	Norm	Conf(%)	Formula		
360.1330	360.13	324	0.6	1.7	11.5	1624.3	n/a	n/a	C19 H17 N3	O F3	



Figure 13. Spectras of compound AK-13

DOCKING

CDK-4- PDB-ID: - 2W96

Coordinates for 2W96 binding site: x = -3.12, y = -3.92, z = 85.1

No docking poses were generated.

BAX-PDB-ID: - 4S0O

Coordinates for 2W96 binding site: x = 11.89, y = 7.0, z = 31.62

Sr. No.	Compound	Docking score
1	AK-10	-2.380
2	AK-3	-1.207



Figure 14: Docking pose of AK-3 (A) and AK-10 (B) with BAX- PDB-ID: 4S00

BCL-XL- PDB-ID: - 6VWC

Coordinates for 2W96 binding site: x = 1.78, y = -4.03, z = 10.8

Sr. No.	Compound	Docking score
1	АК-3	-7.042
2	AK-10	-6.965



Figure 15: Docking pose of AK-3 (A) and AK-10 (B) with **BCL-XL-** PDB-ID: 6VWC

	R ²										
Compound	A549	MCF7	SHSY	НЕК							
AK-1	0.9797	0.9335	1	NA							
AK-2	1	0.9279	0.9941	NA							
AK-3	0.8641	0.952	0.8162	0.785							
AK-4	1	0.9273	0.9762	NA							
AK-5	0.9619	0.9934	0.9478	0.9692							
AK-6	0.9918	0.945	0.9063	NA							
AK-7	0.9975	0.9816	0.9273	NA							
AK-8	0.9661	0.964	0.2599	NA							
AK-9	0.9771	0.9362	0.705	0.899							
AK-10	0.9862	0.9821	0.9978	0.9781							
AK-11	0.9761	0.9074	0.945	NA							
AK-12	0.9856	0.9696	0.9613	NA							
AK-13	0.994	0.9842	0.9974	0.8906							
COLCHICINE	0.9887	0.9753	0.9999	0.9097							

Table 1: R SQUARED VALUES