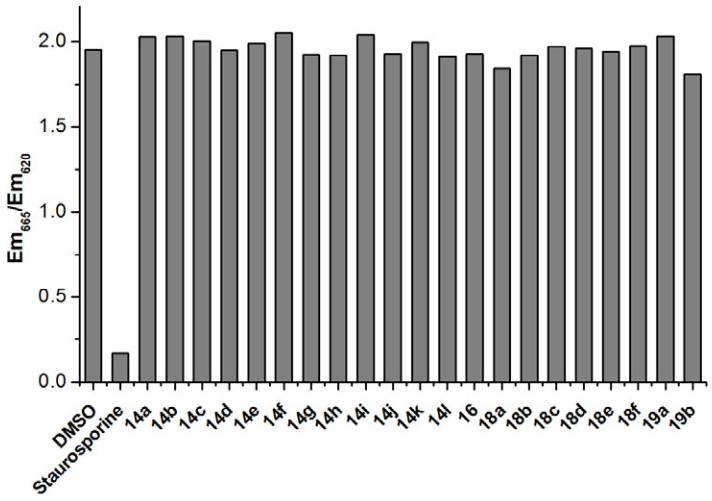
Online supplement to: S. Chakravorty, H.F. Klein, L.E. Hodson, M. Rabillier, Z. Fang, A. Richters, S.C. Pelly, D. Rauh and W.A.L. van Otterlo, *S. Afr. J. Chem.*, 2014, **67**, 71–79.

Figure S1. Compounds **14a–l**, **16**, **18a-f** and **19a** & **b** tested on Abl T315I at 10 µM compound concentrations. **A**) Final emission ratios (Em_{665}/Em_{620}) determined for the respective compounds and controls. **B**) Normalized inhibition rates with respect to DMSO (100%) and Staurosporine (0%).

A)



B)

Abl T315I	
Compound	**Remaining activity (%)**
DMSO	100
Staurosporine	0
14a	104
14b	104
14c	103
14d	100
14e	102
14f	105
14g	98
14h	105
14i	102
14j	99
14k	98
14l	98
16	99
18a	94
18b	98
18b	101
18d	100
18e	99
18f	101
19a	104
19b	92

Abl T315I (0.3 ng/well), purchased from Invitrogen (Lot#39639B, PV3866), was measured with the KinEASE-TK assay from Cisbio according to the manufacturer's instructions. A biotinylated poly-Glu-Tyr substrate peptide was phosphorylated and after completion of the reaction, an anti-phosphotyrosine antibody labeled with europium cryptate and streptavidin labeled with the fluorophore XL665 were added. FRET between europium cryptate and XL665 was measured to quantify the phosphorylation of the substrate peptide. ATP concentrations were set at the K_M value (6 µM) and 250 nM TK-substrate were used. Kinase and inhibitor were preincubated for 30 min before the reaction was started by addition of ATP and substrate peptide. A Tecan infinite M1000 plate reader was used to measure the fluorescence of the samples at 620 nm (Eu-labeled antibody) and 665 nm (XL665 labeled streptavidin) 60 µs after excitation at 317 nm. The experiment was performed in duplicates using plain DMSO as negative control (100% remaining activity) and 10 µM Staurosporine as positive control (0% remaining activity).

Figure S2. Profiling of **14a** at 10 µM compound concentration.

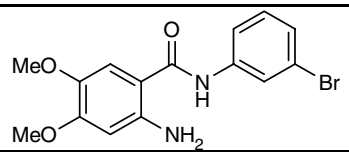
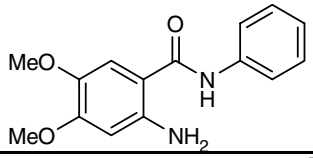
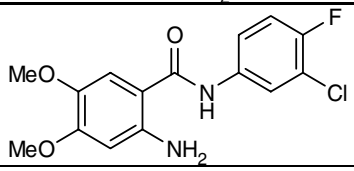
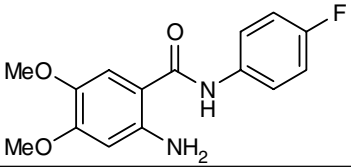
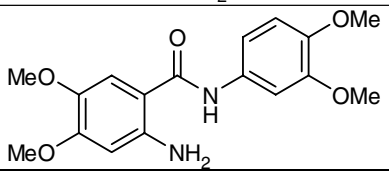
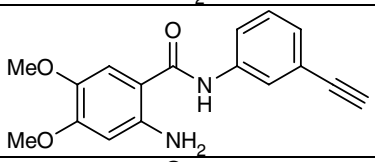
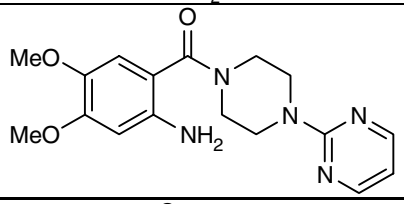
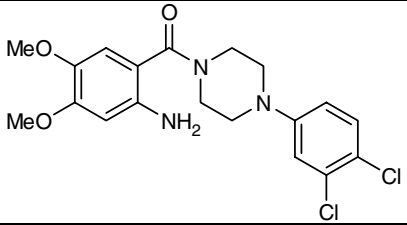
14a					
Kinase	rem. activity (%)	Stdev	Kinase	rem. activity (%)	Stdev
PKBβ	17	0	RSK1	97	2
HER4	43	19	MLK1	97	3
Aurora B	51	11	PAK6	98	3
SRPK1	53	11	MST4	98	4
PIM2	65	0	CK2	99	8
RSK2	67	3	AMPK	99	5
FGF-R1	70	11	EPH A2	99	1
MAPKAP-K3	70	3	IRAK4	100	1
EPH-B3	71	0	CAMKKβ	100	7
CHK2	74	5	ROCK 2	100	2
PLK1	74	3	PAK4	100	2
MINK1	75	2	PKBα	101	1
CAMK1	75	5	PHK	101	11
PIM1	78	2	IR-HIS	101	23
DYRK3	79	1	MELK	102	2
TTK	79	1	p38δ MAPK	102	9
VEG-FR	80	13	RIPK2	103	2
BRSK2	83	8	PRK2	103	7
PKD1	83	1	CDK2-Cyclin A	103	0
TBK1	85	1	p38γ MAPK	104	5
DYRK2	86	1	CHK1	104	1
IGF-1R	86	14	IKKβ	104	18
MST2	88	1	p38β MAPK	105	6
MNK1	88	9	PKCζ	105	3
HIPK3	88	12	ERK8	105	8
MKK1	89	7	BRSK1	106	9
PIM3	90	25	PDK1	106	0
MARK3	91	4	ERK1	106	12
BTK	91	9	PAK2	107	16
PAK5	91	3	S6K1	107	8
HIPK2	92	9	Src	107	2
Aurora A	92	3	JNK2	107	4
MARK4	92	5	LKB1	108	3
NUAK1	93	6	IRR	108	7
GSK3β	93	9	ERK2	109	6
DYRK1A	94	1	CSK	109	5
NEK6	94	6	MLK3	111	1
YES1	94	4	PRAK	111	23
PKA	94	1	Lck	113	6
PKCα	94	4	MARK2	114	1
NEK2a	94	6	CK1	114	13
SmMLCK	95	8	JNK3	115	5
GCK	96	3	MAPKAP-K2	115	5
SGK1	96	1	IKKε	116	9
JNK1	96	3	SYK	119	4
HIPK1	97	0	MNK2	119	7
MSK1	97	14	EF2K	123	1
p38α MAPK	97	7			

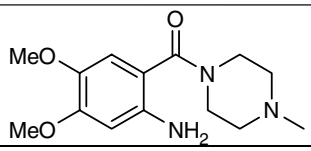
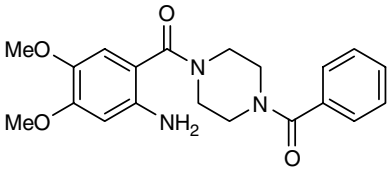
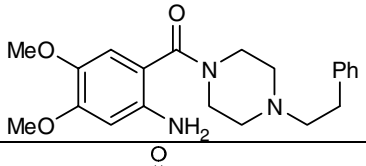
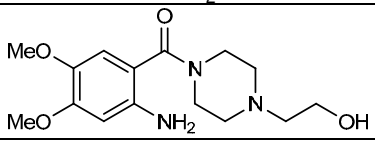
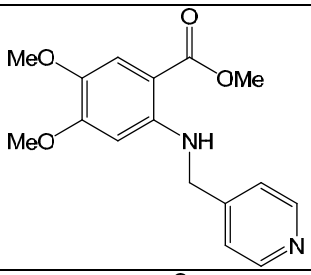
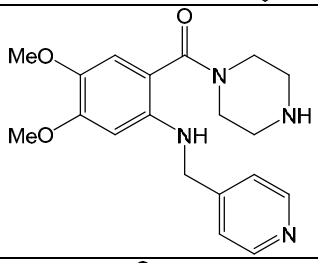
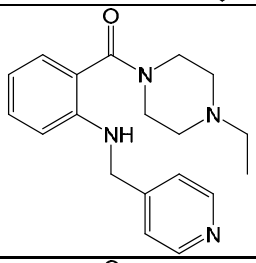
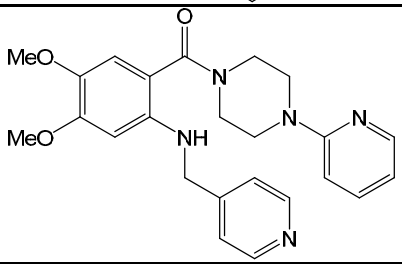
Figure S3. Profiling of **14h** at 10 µM concentration.

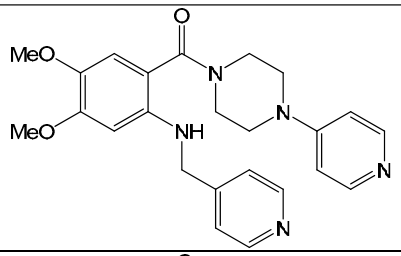
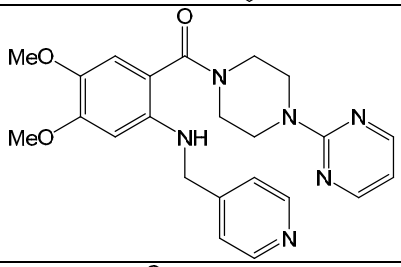
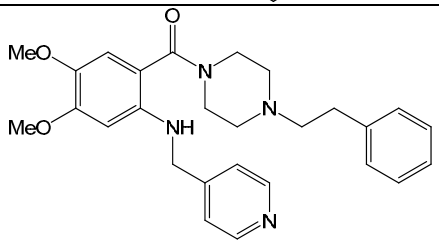
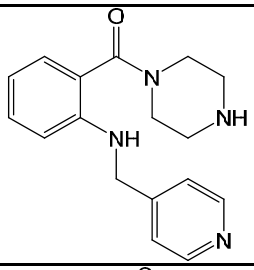
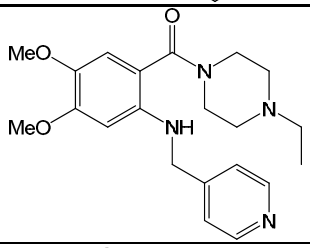
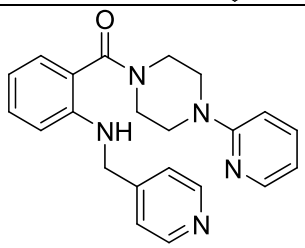
14h					
Kinase	rem. activity (%)	Stdev	Kinase	rem. activity (%)	Stdev
CAMK1	60	9	Lck	86	6
Aurora B	61	18	TBK1	86	2
PKBβ	64	4	p38β MAPK	86	6
MNK1	67	12	IRAK4	86	5
CHK2	71	8	MAPKAP-K2	87	1
HER4	71	10	MKK1	87	12
MAPKAP-K3	72	9	ROCK 2	87	5
PIM1	73	9	IGF-1R	88	0
FGF-R1	74	3	JNK1	88	6
NUAK1	74	3	IKKε	88	10
SmMLCK	75	2	PKD1	88	15
HIPK3	76	1	CK2	88	1
PIM2	76	1	CK1	89	4
MINK1	77	1	DYRK1A	89	3
YES1	78	13	S6K1	89	7
PLK1	78	6	NEK2a	89	7
BRSK2	78	3	EPH-B3	90	3
RSK2	79	2	DYRK3	90	3
p38δ MAPK	80	2	RIPK2	90	1
PAK6	80	9	MLK3	90	2
BTK	80	3	CAMKKβ	90	1
MST2	81	8	AMPK	91	3
PKA	82	3	PAK2	91	5
VEG-FR	82	5	p38α MAPK	91	1
SRPK1	82	15	IR-HIS	91	16
SYK	82	5	IKKβ	91	3
ERK1	82	2	SGK1	92	11
HIPK1	82	6	HIPK2	92	12
MARK2	82	11	MST4	92	3
NEK6	82	4	RSK1	93	0
DYRK2	82	1	MSK1	94	3
MELK	83	17	JNK2	94	3
PIM3	83	16	IRR	95	3
MLK1	83	15	CDK2-Cyclin A	95	12
BRSK1	83	8	PRK2	96	2
PRAK	83	0	PKCα	97	5
JNK3	83	9	LKB1	97	0
PAK4	84	3	PDK1	97	11
Src	84	2	MARK3	97	13
PAK5	84	0	ERK2	98	2
MNK2	84	2	Aurora A	98	9
GSK3β	84	7	p38γ MAPK	99	2
CHK1	84	2	PKCζ	99	1
ERK8	85	1	EF2K	103	1
GCK	85	1	PHK	104	6
CSK	85	4	MARK4	109	24
EPH A2	86	5	PKBα	121	5
TTK	86	2			

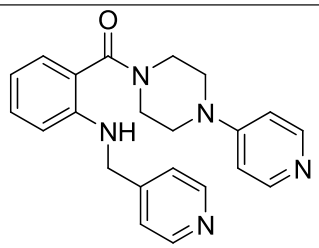
14a and **14h** were tested on 95 kinases at 10 µM concentrations using a radiometric (^{33}P-γ-ATP) filter-binding assay conducted at the MRC Protein Phosphorylation Unit of the University of Dundee (http://www.kinase-screen.mrc.ac.uk/). ATP concentrations were chosen individually for each kinase to be at their respective ATP-Km. The remaining activity of each kinase was normalized and is represented in %.

Figure S4. Table containing testing of "library 1" (compounds **14a-l**) and "library 2" (compounds **18a-f** and **19a-d**) against kinases Akt1 and Akt2. [n.i. = no inhibition up to 100 µM. All experiments were conducted in duplicate in three independent measurements (n = 3)].

structure	name	no	% activity @ 100 µM			IC_{50} / µM		
			Akt1	ΔPH-Akt1	Akt2	Akt1	ΔPH-Akt1	Akt2
	WvO-1b	**14a**	79 ± 8	102 ± 8	128 ± 9	n.i.		n.i.
	WvO-1c	**14b**	82 ± 13	109 ± 11	120 ± 14			
	WvO-2b	**14c**	72 ± 7	112 ± 10	120 ± 5	n.i.	n.i.	n.i.
	WvO-2c	**14d**	101 ± 25	108 ± 11	123 ± 2			
	WvO-3b	**14e**	104 ± 13	110 ± 13	130 ± 10	n.i.		n.i.
	WvO-4b	**14f**	69 ± 7	104 ± 8	128 ± 12	n.i.		n.i.
	WvO-5b	**14g**	101 ± 11	102 ± 4	127 ± 3	n.i.		n.i.
	WvO-10b	**14h**	85 ± 19	101 ± 7	109 ± 2	n.i.		n.i.

	WvO-8b	**14i**	85 ± 19	106 ± 12	122 ± 5			
	WvO-6b	**14j**	83 ± 12	110 ± 4	122 ± 1		n.i.	
	WvO-9b	**14k**	80 ± 19	100 ± 15	125 ± 5	n.i.		n.i.
	WvO-11b	**14l**	93 ± 18	103 ± 11	122 ± 12			
	WvO-HFK1	**16**	92 ± 13	105 ± 8	126 ± 1			
	WvO-SC3	**18a**	100 ± 11	89 ± 17	128 ± 22			
	WvO-SC2	**18b**	109 ± 13	102 ± 4	108 ± 13	n.i.		n.i.
	WvO-HFK3	**18c**	91 ± 14	86 ± 15	134 ± 7	n.i.		n.i.

	WvO-HFK4	**18d**	66 ± 6	72 ± 12	95 ± 8	n.i.	n.i.	n.i.
	WvO-HFK5	**18e**	83 ± 0,5	106 ± 3	151 ± 5			
	WvO-HFK13	**18f**	93 ± 5	101 ± 4	89 ± 4	n.i.		n.i.
	WvO-SC4	**19a**	113 ± 8	103 ± 7	98 ± 4	n.i.		n.i.
	WvO-SC5	**19b**	90 ± 16	103 ± 2	87 ± 1	n.i.		n.i.
	WvO-HFK4-2	**19c**	100 ± 19	104 ± 10		n.i.		n.i.

	WvO-HFK4-1	**19d**	81 ± 20	105 ± 6		n.i.		n.i.