Supplementary Material (ESI) for Organic & Biomolecular Chemistry

Supporting Information for

Synthesis, Characterization and Antioxidant Activity of Angiotensin Converting Enzyme Inhibitors

by

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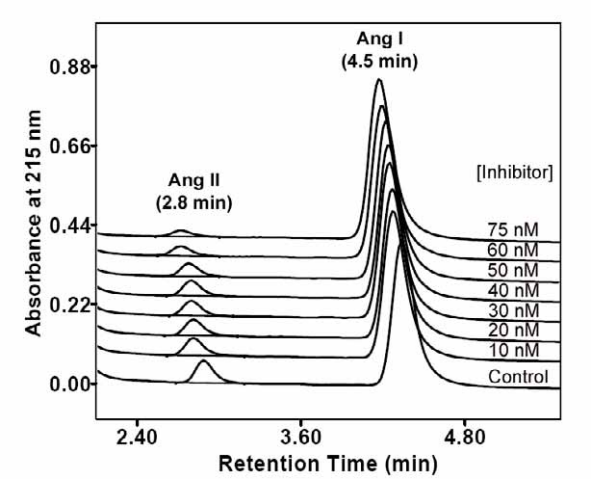

Figure S1. HPLC chromatograms for the ACE inhibition by compound **5.**

Table S1: IC_{50} values for inhibition of ACE by compounds **1**, **5-11.**

Compound	IC_{50} (nM)	Compound	IC_{50} (nM)
1	18.1 ± 1.0	**5**	36.4 ± 1.5
6	7500 ± 500	**7**	5300 ± 440
8	30000[a]	**9**	342 ± 33

10	6480 ± 640	**11**	50000[b]

[a]30% enzyme activity was inhibited at 30000 nM inhibitor concentration. [b]40% enzyme activity was inhibited at 50000 nM inhibitor concentration.

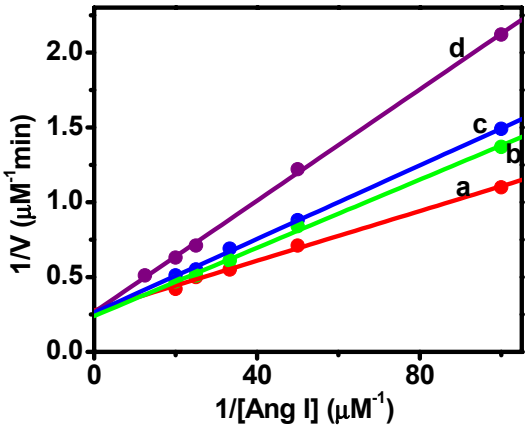

Figure S2. Lineweaver-Burk plots obtained for compound **5** at various concentrations of Ang I and fixed concentration of the inhibitor. a) inhibitor = 0 nM, b) Inhibitor = 25 nM, c) Inhibitor = 40 nM, and d) inhibitor = 55 nM.

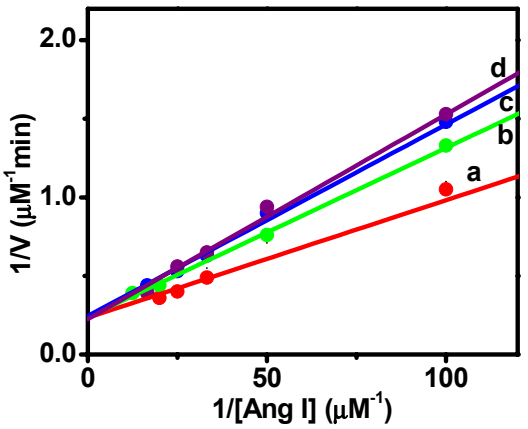

Figure S3. Lineweaver-Burk plots obtained for compound **6** at various concentrations of Ang I and fixed concentration of the inhibitor. a) inhibitor = 0 nM, b) Inhibitor = 500 nM, c) Inhibitor = 7500 nM, and d) inhibitor = 10000 nM.

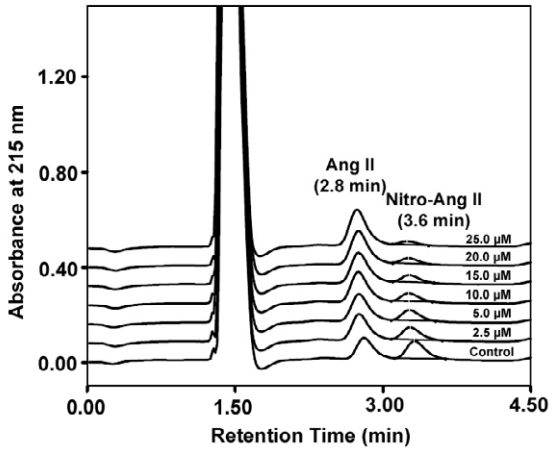

Figure S4: HPLC chromatogram for inhibition of PN-mediated nitration of Ang II.

Table S2: IC_{50} values for inhibition of PN-mediated nitration of Ang II by compounds **1**, **5-11, 15, 18, 25, 26, 35, 36, 41 and 42.**

Compound	IC_{50} (µM)	Compound	IC_{50} (µM)
1	25.6 ± 0.9	**42**	33.2 ± 0.2
5	2.2 ± 0.1	**15**	11.0 ± 0.1
6	2.3 ± 0.1	**18**	11.8 ± 0.7
7	6.4 ± 0.5	**25**	16.1 ± 0.7
8	9.1 ± 0.1	**26**	5.2 ± 0.3
9	7.5 ± 0.4	**35**	3.8 ± 0.2
10	14.8 ± 1.0	**36**	49.1 ± 4.1
11	9.5 ± 0.1	**41**	6.8 ± 0.6

X-ray Crystallography: X-ray crystallographic studies were carried out on a Bruker CCD diffractometer with graphite-monochromatized Mo- Kα radiation (λ = 0.71073 Å) controlled by a Pentium-based PC running on the SMART software package.[S1] Single crystals were mounted at room temperature on the ends of glass fibers and data were collected at room temperature. The structures were solved by direct methods and refined using the SHELXTL software package.[S2] All non-hydrogen atoms were refined anisotropically and hydrogen atoms were assigned idealized locations. Empirical absorption corrections were applied to all structures using

SADABS.[S3] The structures were solved by direct method (SIR-92) and refined by full-matrix least-squares procedure on F2 for all reflections (SHELXL-97).[S4]

Table S3. The crystallographic details of compounds **13, 15** and **20**.

Compound	**13**	**15**	**20**
Crystal Data			
Empirical Formula	$C_{21}H_{36}BrN_2O_3$	$C_{18}H_{26}N_2O_6Se_2$	$C_{10}H_{12}O_3Se$
Formula Weight	444.43	524.33	259.16
Crystal System	Triclinic	Monoclinic	Orthorhombic
Space group	P1	$P2_1$	$P2_1ab$
a, b, c [Å]	5.3658 (11)	6.9783 (3)	5.7334 (9)
	10.1748 (18)	11.2514 (5)	7.8990 (12)
	10.905 (2)	14.4801 (7)	47.642 (7)
α, β, γ [deg]	82.918 (11)	90.00	90.00
	88.385 (11)	91.389 (2)	90.00
	78.119 (12)	90.00	90.00
V [$Å^3$]	578.16 (19)	1136.58 (9)	2157.6 (6)
Z	1	2	8
ρ_{calc} [g/cm^3]	1.276	1.532	1.596
Data Collection			
Temperature (K)	296 (2)	296 (2)	293 (2)
Radiation [Å] MoK_α	0.71073	0.71073	0.71073
Theta Min-Max [°]	1.88, 25.44	2.29, 23.14	1.71, 28.01
Tot., Uniq. Data	7602, 3881	10037, 3024	17521, 5061
Observed data [$I>2\sigma(I)$]	1812	2350	3676
Flack parameter	0.21 (3)	0.036 (15)	
Refinement			
N_{ref}, N_{par}	3881, 255	3024, 255	5061, 253
R_1(Obs data)[a]	0.095	0.044	0.053
wR_2 (Obs data)[b,c]	0.266	0.093	0.079
R_1(All data)[a]	0.179	0.064	0.119
wR_2 (All data)[b,c]	0.302	0.100	0.130
S	0.921	1.036	1.019

Max. and Av.	0.001, 0.000	0.004, 0.000	0.612, 0.086
Min. and Max. resd. dens. [e/Å^3]	-0.362, 0.878	-0.292, 0.526	-0.542, 0.506

$^a R = \sum||F_o| - |F_c||/\sum|F_o|$; $^b R_w = \{\sum[w(|F_o| - |F_c|)^2]/\sum[wF_o^2]\}^{1/2}$; $^c w = 1/\sigma^2(F_o)$.

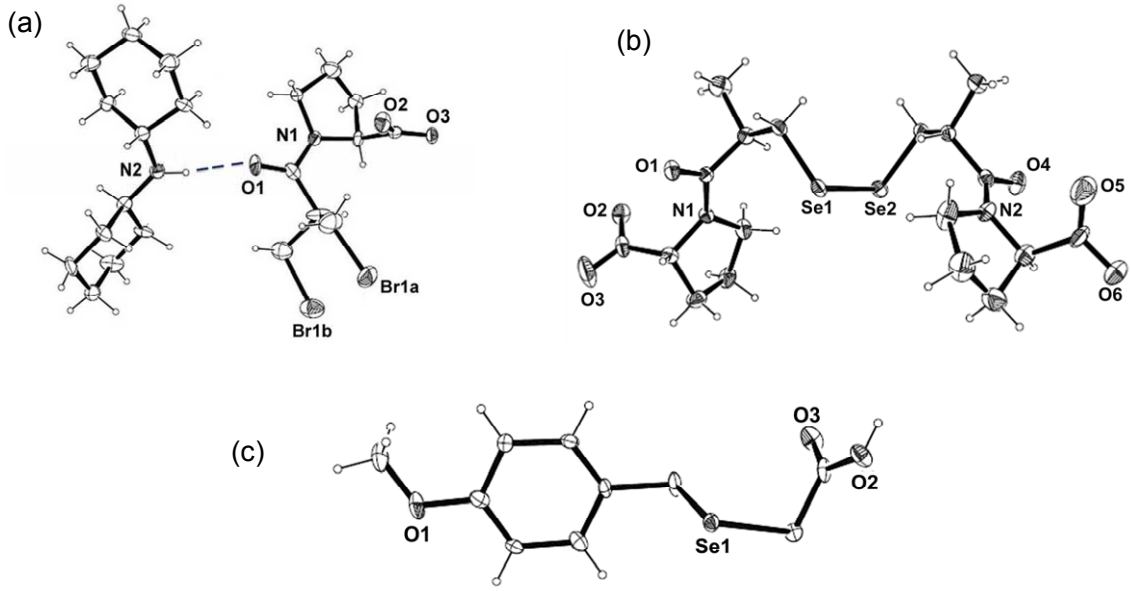

Figure S5: X-ray crystal structure of (a) compound **13**, (b) compound **15** and (c) compound **20**. ORTEP diagram with the ellipsoids representing 50% probability.

References:

S1 SMART, Version 5.05, Bruker AXS, Madison, WI, **1998**.

S2 (a) Sheldrick, G. M. *Acta Crystallogr. Sect. A* **1990**, *46*, 467-473. (b) Altomare, A.; Cascarano, G.; Giacovazzo, C.; Gualardi, A. *J. Appl. Cryst.* **1993**, *26*, 343-350.

S3 Sheldrick, G. M. SADABS, A program for absorption correction with the siemens SMART area-detector system, University of Göttingen, Germany, **1996.**

S4 Sheldrick, G. M. SHELX-97, Program for the Refinement of Crystal Structures, University of Göttingen, Germany, **1997**.