Electronic Supplementary Material (ESI) for Organic & Biomolecular Chemistry.

Supplementary Information

Synthesis and biochemical evaluation of two novel N-hydroxyalkylated cyclosporin A analogs

Viktoria Kahlert, Erik Prell, Oliver Ohlenschläger, Jelena Melesina, Michael Schumann, Christian Lücke, Gunter Fischer and Miroslav Malešević

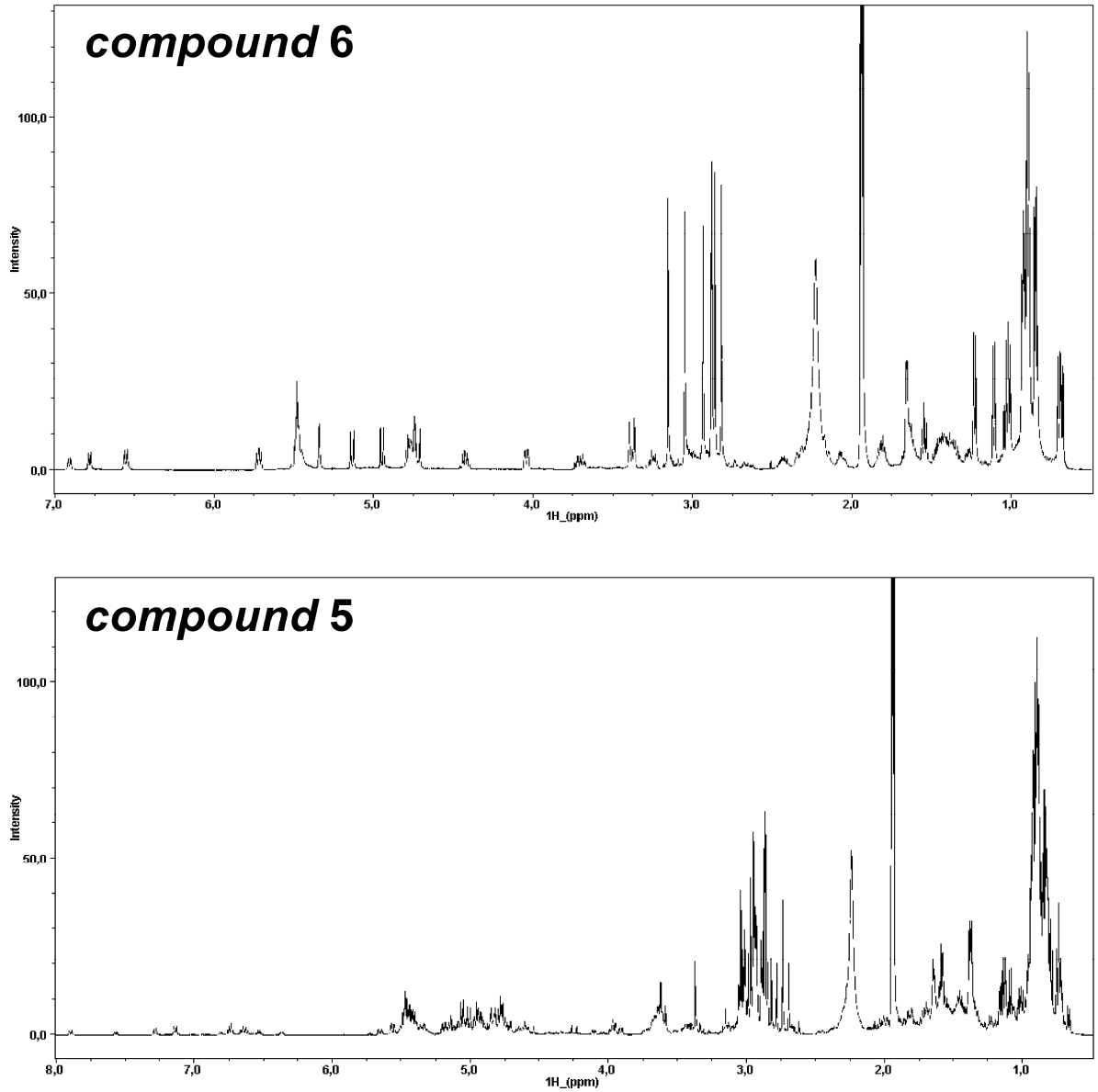

Figure S1: One-dimensional ^{1}H-NMR spectra of compounds **6** (upper panel) and **5** (lower panel) in CD_3CN. (Figure produced with NMRViewJ from One Moon Scientific.)

Table S1: ^{1}H- and ^{13}C resonance assignments of compound **6** at 25 °C in CD_3CN:

residue	NH/NCH_3	CO	CαH	CβH	CγH	CδH	CεH	CζH	CηH
MeBmt1	2.93(35.3)	171.8	5.34(59.1)	4.04(76.9)	1.44(36.8)	2.33/2.07(36.7)	5.48(129.7)	5.48(127.7)	1.65(18.2)
					0.83(15.8)				
Abu2	6.78(-)	175.5	4.76(53.1)	1.80/1.63(24.6)	1.03(10.8)				
Sar3	3.15(37.4)	169.2	4.73/3.38(51.1)						
MeLeu4	2.82(29.5)	172.0	5.72(51.2)	1.65/1.47(38.9)	1.38(25.3)	0.92(23.3)			
						0.89(23.1)			
Val5	3.38/3.24(61.8)								
	3.70/3.01(45.0)	173.9	5.13(58.6)	2.43(27.9)	0.85(20.4)				
					0.68(18.1)				
MeLeu6	2.86(30.9)	170.6	4.79(55.4)	1.81/1.41(36.4)	1.41(25.5)	0.91(23.2)			
						0.91(22.8)			
Ala7	6.55(-)	172.3	4.42(48.3)	1.11(17.4)					
D-Ala8	6.90(-)	173.4	4.74(45.8)	1.23(16.9)					
MeLeu9	2.88(30.5)	172.2	5.48(52.6)	1.54(38.5)	1.35(25.2)	0.89(23.4)			
						0.89(22.7)			
MeLeu10	3.04(32.4)	173.6	5.46(52.6)	2.17/1.26(38.6)	1.62(25.6)	1.01(24.2)			
						0.92(21.2)			
MeVal11	2.88(30.5)	171.7	4.94(59.2)	2.27(27.1)	0.85(20.3)				
					0.70(18.3)				

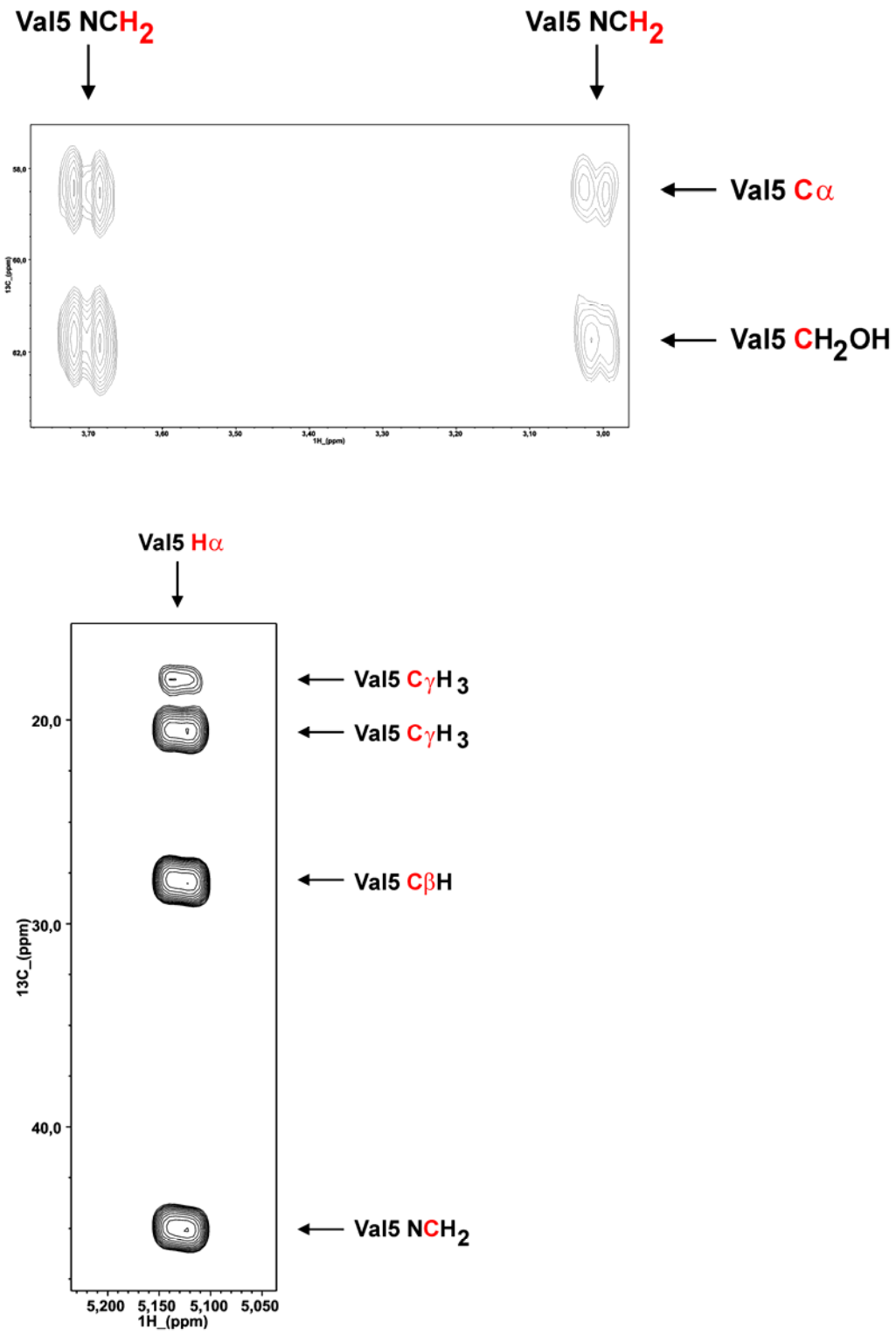

Figure S2: Segments from the $^{1}H/^{13}C$-HMBC spectrum of compound **6**, showing the scalar through-bond connectivities i) of the methylene protons in the ethoxy moiety attached to the Val5 nitrogen atom (upper panel) and ii) of the Val5 Cα proton (lower panel). (Figure produced with NMRViewJ from One Moon Scientific.)

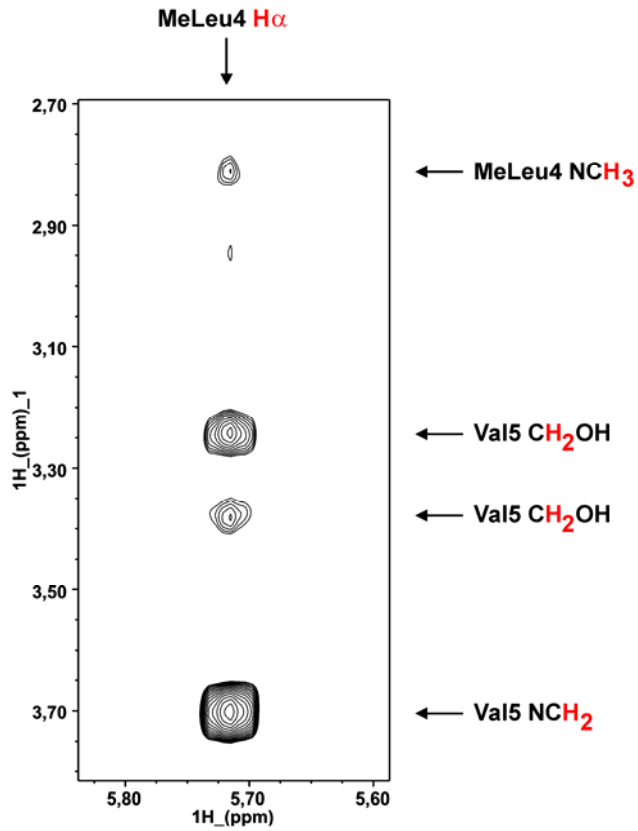

Figure S3: Segments from the ^{1}H/^{1}H-ROESY spectrum of compound **6**, showing the dipolar through-space connectivities of the MeLeu4 Cα proton with the protons of the ethoxy moiety attached to the Val5 nitrogen atom. (Figure produced with NMRViewJ from One Moon Scientific.)

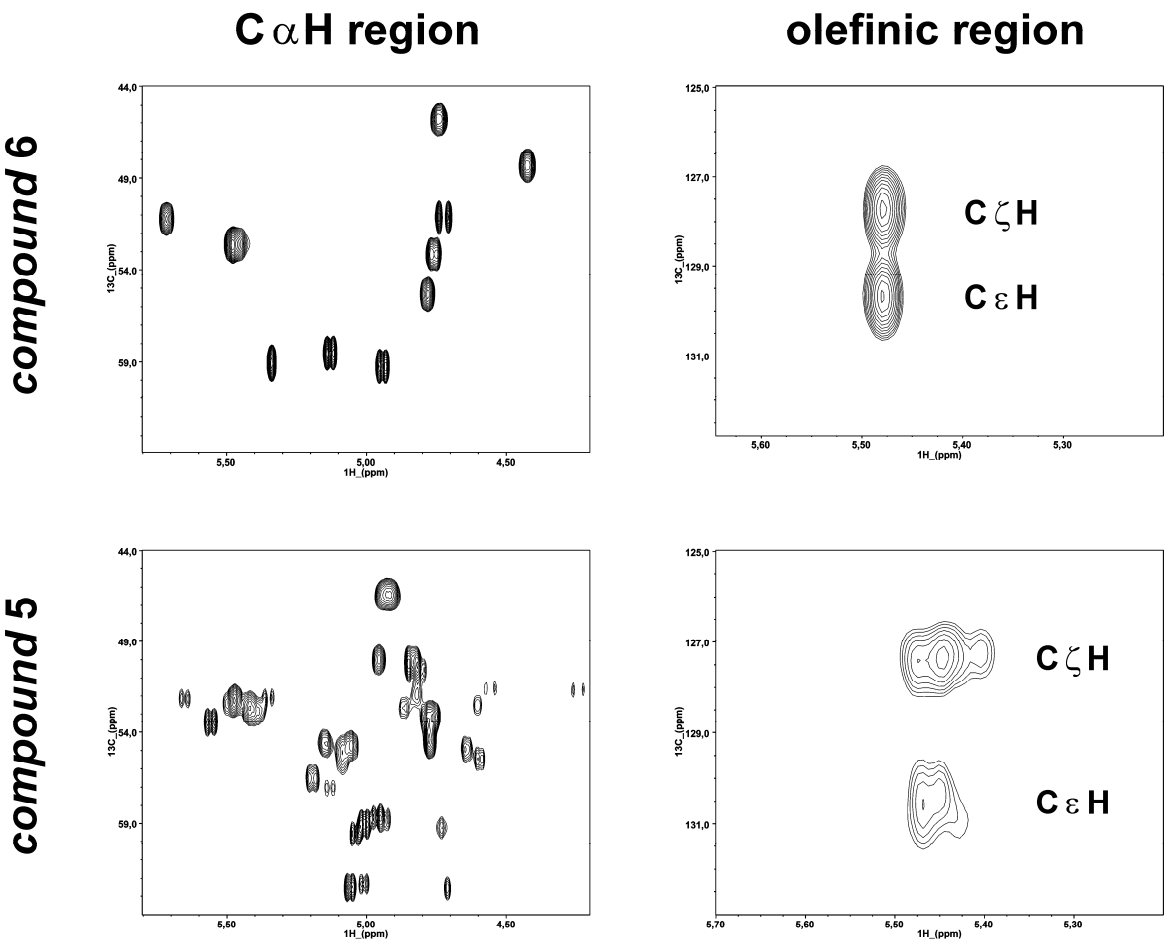

Figure S4: Sections from the two-dimensional $^{1}H/^{13}C$-HSQC spectra of compounds **6** (upper panels) and **5** (lower panels). The panels on the left show the CαH region, characterized by 11 peaks in case of compound **6** (the Sar3 Hα resonance at 3.38 ppm is not shown in this plot), whereas the same region in the spectrum of compound **5** displays a considerably larger number of signals. The panels on the right show another example of this heterogeneity of ^{1}H resonances in case of the two olefinic protons (CεH and CζH) of the MeBmt1 residue. (Figure produced with NMRViewJ from One Moon Scientific.)

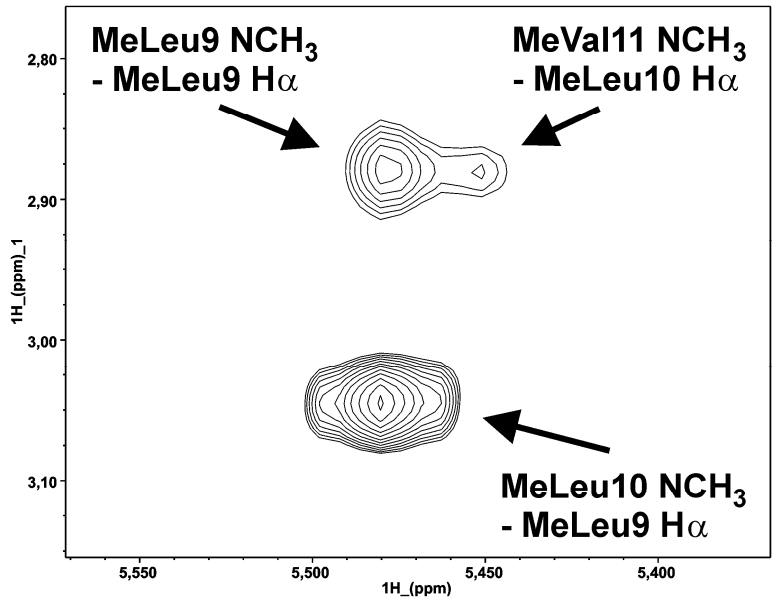

Figure S5: Segment from the $^{1}H/^{1}H$-ROESY spectrum of compound **6** showing among others the very strong sequential ROE signal between MeLeu9 Hα and MeLeu10 NCH_3. (Figure produced with NMRViewJ from One Moon Scientific.)

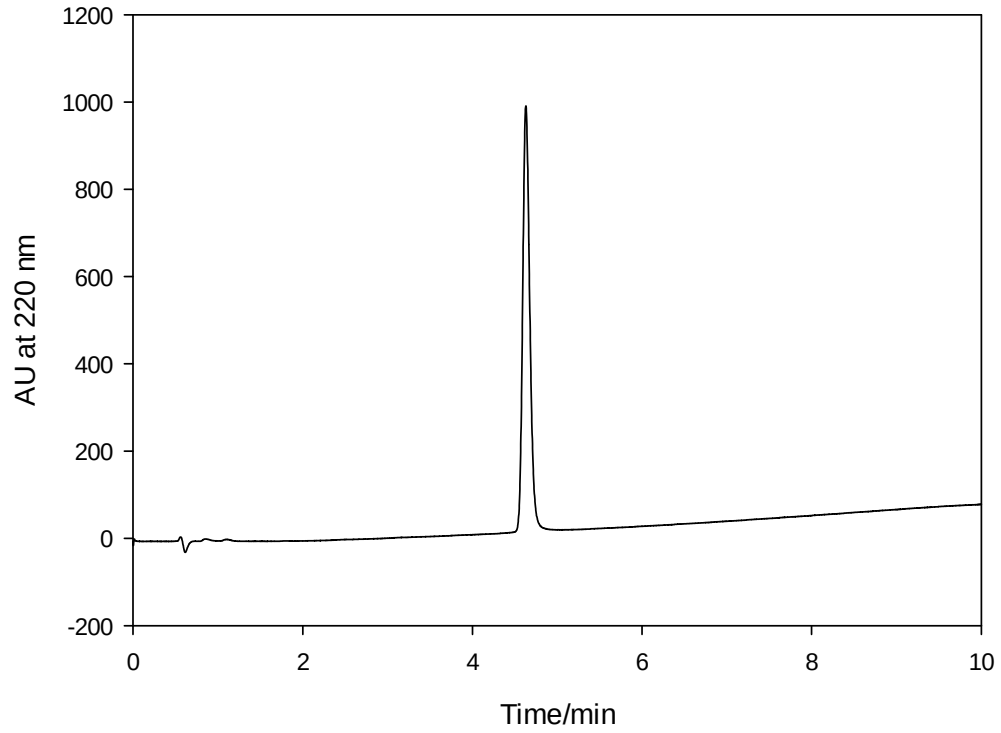

Figure S6: HPLC chromatogram of purified compound **5** Rt = 4.6 min (solvent A H_2O, solvent B acetonitrile, RP C8, 50.00 x 4.60 mm. Method: 40 °C, 50 – 100 % B in 10 min, flow 1 mL/min).

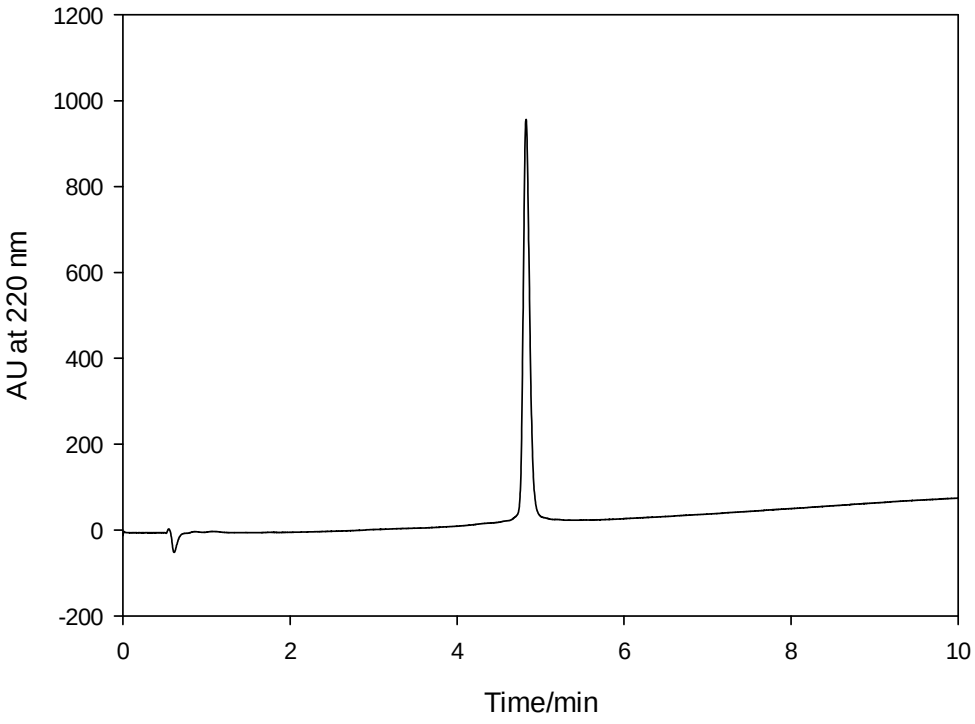

Figure S7: HPLC chromatogram of purified compound **6** Rt = 4.8 min (solvent A H_2O, solvent B acetonitrile, RP C8, 50.00 x 4.60 mm. Method: 40 °C, 50 – 100 % B in 10 min, flow 1 mL/min).