

Supporting Information

The ⁶⁸Ga-complex lipophilicity and the targeting property of a urea based PSMA inhibitor for PET imaging

Matthias Eder[†], Martin Schäfer[†], Ulrike Bauder-Wüst[†], William-Edmund Hull[‡], Carmen Wängler[§], Walter Mier[§], Uwe Haberkorn[§], Michael Eisenhut[†]

[†] Radiopharmaceutical Chemistry, German Cancer Research Center, Heidelberg, Germany

[‡] Molecular Structure Analysis, German Cancer Research Center, Heidelberg, Germany

[§] Department of Nuclear Medicine, University Hospital Munich, Munich, Germany

[§] Department of Nuclear Medicine, University of Heidelberg, Heidelberg, Germany

Corresponding author

Dr. Matthias Eder

Radiopharmaceutical Chemistry, German Cancer Research Center

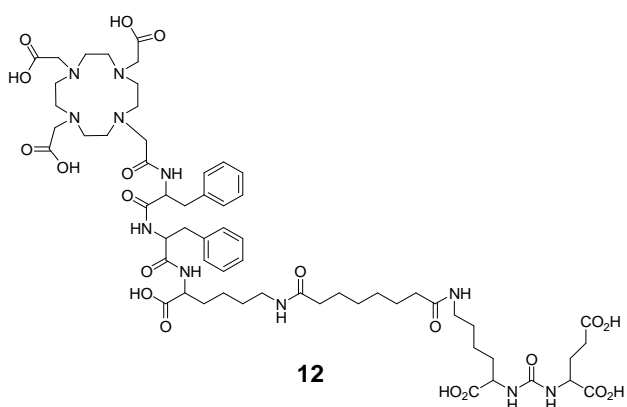
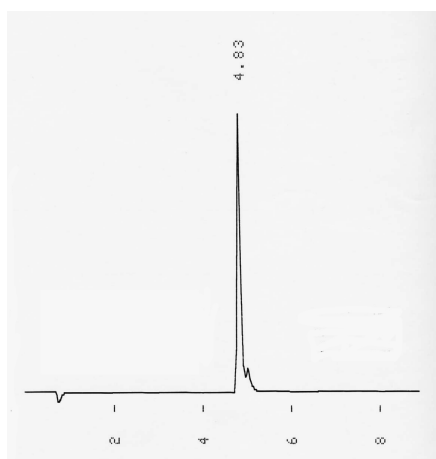
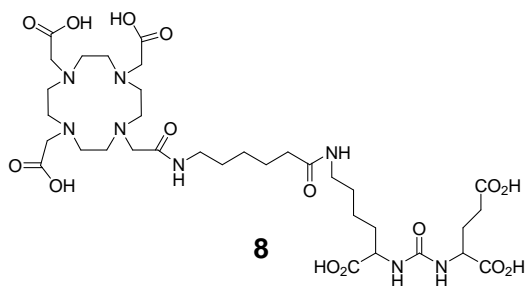
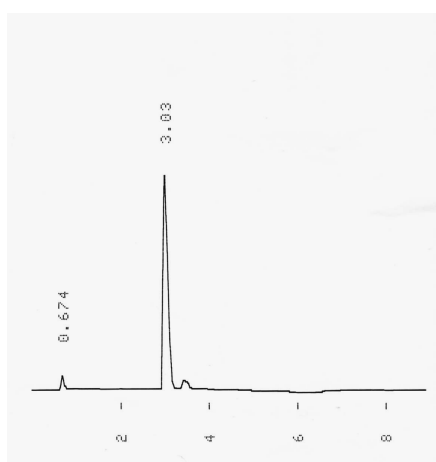
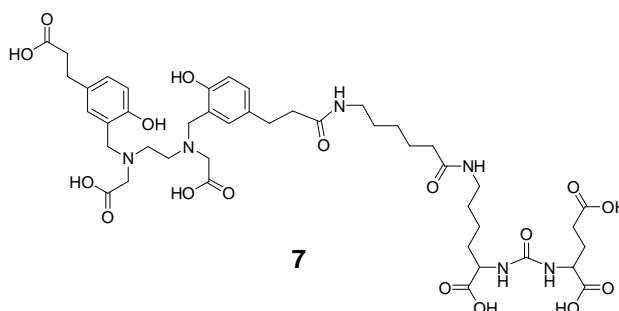
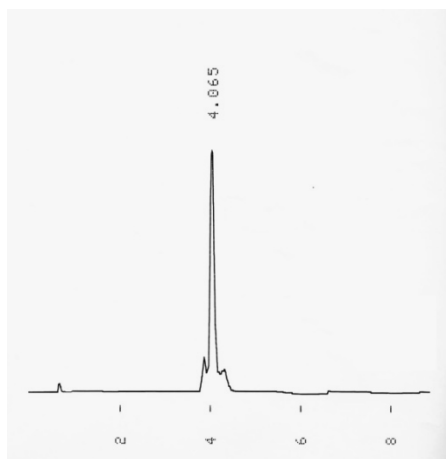
Im Neuenheimer Feld 280

69120 Heidelberg, Germany

Telephone 00496221422691 Fax 00496221422690

e-mail: m.eder@dkfz.de

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HPLC runs of compounds **7**, **8** and **12** using Chromolith RP-18e column, 100x4.6 mm (Merck, Darmstadt, Germany). Analyses were performed using a linear gradient of 100% aqueous TFA (0.1%) to 100% methanol (0.1% TFA) in 7 min at a flow rate of 2.8 mL/min. Chromatograms were recorded at 206 nm and base line corrected. Small satellite peaks which indicate potential impurities could not be removed by HPLC even after stringent collection of the peak tops.

8 in DMSO-d6, NMR #31122 @ 400.13 MHz for 1H

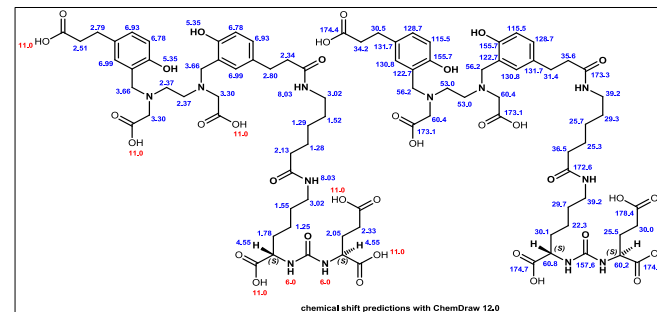
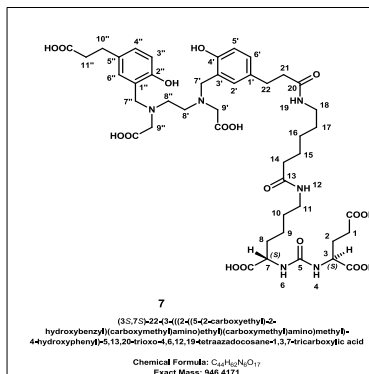
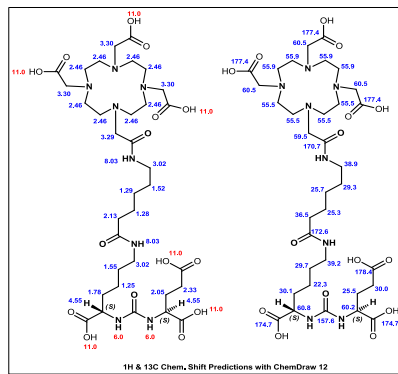
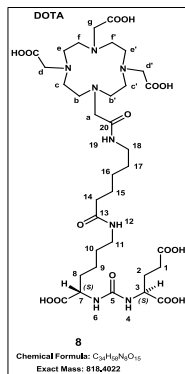
Measurements	Temperature	Time
1D 1H	303, 313, 333, 348 Kelvin	2 h
1D 13C	348 K, 1H-decoupled	12 h
2D COSY-45	348 and 303 K	2h, 2h
2D T-ROESY (Overhauser, 300 ms)	348 K	4h
1H/13C-HSQC	348 and 303 K	7.8 h, 2 h
1H/13C-HMBC (8 Hz opt.)	348 and 303 K	7.9 h, 13.5 h

7 in DMSO-d6, NMR #31085 @ 600.13 MHz for 1H

Measurements	Temperature	Time
1D 1H	303 K	0.5 h
1D 13C (1H-decoupled, DEPT-135)	303 K	20 h, 6 h
2D COSY-45	303 K	4.2 h
2D T-ROESY (Overhauser, 300 ms)	303 K	13 h
1H/13C-HSQC	303 K	8.5 h
1H/13C-HMBC (8 Hz opt.)	303 K	14 h

For both compounds, complete and unequivocal 1H and 13C signal assignments were obtained through the 2D experiments. The DOTA derivative 8 was measured at 400 MHz and 348K to achieve fast-exchange averaging of DOTA conformations and resolution of all chemical shifts. Where possible chem. shifts were taken from 1D spectra, when necessary from 2D spectra; 1H coupling constants were estimated by simple 1st-order analysis of multiplets.

Instruments used: Bruker Avance NMR Spectrometers, AV(I)-600 (600 MHz) and AV(III)-400 (400 MHz), 5-mm sample tubes. Chem. Shifts are referenced to solvent signals (DMSO-d5 = 2.50 / 39.757 ppm, DMSO-d6 = 39.50) at all temperatures.



Compound 8, 348K in DMSO-d6

Pos.	13C Shift	1H Shift	multiplicity	J(H,H) couplings at 348K
1a	29,722	2,232	ddd	-16.4 (1a,1b); 6.2 (1a,2a); 8.7 (1a,2b)
1b	2,285	2,285	ddd	8.9 (1b,2a); 7.1 (1b,2b)
2a	27,387	1,759	ddd	-13.8 (2a,2b); 8.4 (2a,3)
2b	1,948	1,948	ddd	5.3 (2b,3)
3	51,607	4,134	ddd br	NR
4	6,273	d br	d br	7.6 (3,4)
5	157,026			
6	6,231	d br	d br	7.6 (6,7)
7	52,150	4,077	ddd br	NR
8a	31,607	1,532	ddd	NR
8b	1,672	1,672	ddd	-13.4 (8a,8b); 5.6 (7,8b); 7.8 (8b,9)
9	22,304	1,312	ddt	NR
10	28,510	1,414	tt	NR
11	38,062	3,023	dt	NR
12	7,504	t br	t br	5.6 (11,12)
13	171,655			
14	35,043	2,058	t	7.4 (14,15)
15	24,565	1,510	tt	7.5 (15,16)
16	25,789	1,273	tt	NR
17	28,200	1,469	tt	NR
18	38,374	3,105	dt	NR
19	8,120	t br	t br	5.3 (18,19); 6.8 (17,18)
20	166,279			
a	55,023	3,677	s br	
b,b'	50,984	3,170	t br	5 br (b,c)
c,c'	49,155	3,051	t br	NR
d,d'	53,686	3,610	s br	
e,e'	49,466	3,020	t br	NR
f,f'	50,606	3,196	t br	NR
g	54,046	3,754	s br	
1-COOH	173,131	C	v br	
3-COOH	173,469	C	v br	
7-COOH	173,862	C	v br	
d,d'-COOH	170,887	C	v br	
e'-COOH	169,969	C	v br	

Compound 8, 303K in DMSO-d6

Pos.	13C Shift	1H Shift	multiplicity	J(H,H) couplings at 303K
1a	29,907	2,209	ddd	-16.6 (1a,1b); 6.1 (1a,2a); 8.85 (1a,2b)
1b	2,268	2,268	ddd	9.0 (1b,2a); 7.2 (1b,2b)
2a	27,521	1,709	ddd	-13.9 (2a,2b); 8.3 (2a,3)
2b	1,916	1,916	ddd	5.2 (2b,3)
3	51,678	4,091	ddd	
4	6,359	d	d	8.2 (3,4)
5	157,265			
6	6,323	d	d	8.2 (6,7)
7	52,283	4,033	ddd	8.1 (7,8a); 5.3 (7,8b)
8a	31,788	1,501	ddd	
8b	1,638	1,638	ddd	
9	22,630	1,268	ddt	
10	28,814	1,375	tt	
11	38,286	2,996	dt	7.1 (10,11)
12	7,750	t	t	5.6 (11,12)
13	171,890			
14	35,269	2,038	t	7.4 (14,15)
15	24,938	1,475	tt	
16	26,066	1,238	tt	
17	28,969	1,416	tt	
18	38,679	3,082	dt	
19	8,381	t br	t br	
20	165,603			
a	54,881	3,788	s br	
b,b'	50,730	3,237	t br	
c,c'	48,693	3,059	t br	
d,d'	53,088	3,590	s br	
e,e'	48,693	ND	br	
f,f'	50,550	ND	br	
g	54,087	3,910	s br	
1-COOH	173,630	12,35	v br	
3-COOH	174,050	12,35	v br	
7-COOH	174,440	12,35	v br	
d,d'-COOH	171,538	12,35	v br	
e'-COOH	ND	12,35	v br	
-NHx	unknown	7,2607	s br	integral = 0.44
-NHx	unknown	6,6462	s br	integral = 0.37

Compound 7, 303K in DMSO-d6

Pos.	13C Shift	1H Shift	multiplicity	J(H,H) couplings
1a	29,868	2,221	ddd	-16.5 (1a,1b); 5.8 (1a,2a); 9.2 (1a,2b)
1b	2,256	2,256	ddd	9.1 (1b,2a); 6.7 (1b,2b)
2a	27,506	1,710	ddd	-13.9 (2a,2b); 8.3 (2a,3)
2b	1,918	1,918	ddd	5.2 (2b,3)
3	51,635	4,095	ddd	
4	6,324	d	d	8.3 (3,4)
5	157,266			
6	6,288	d	d	8.2 (6,7)
7	52,239	4,038	ddd	8.1 (7,8a); 5.2 (7,8b)
8a	31,781	1,506	ddd	
8b	1,633	1,633	ddd	
9	22,600	1,265	ddt	
10	28,816	1,373	tt	
11	38,269	2,994	dt	7.1 (10,11)
12	7,719	t	t	5.7 (11,12)
13	171,887			
14	35,229	2,017	t	7.5 (14,15)
15	25,013	1,452	tt	7.5 (15,16)
16	26,110	1,178	tt	
17	28,966	1,340	tt	7.6 (16,17)
18	38,353	2,990	dt	7.1 (17,18)
19	7,745	t	t	5.7 (18,19)
20	171,248			
21	37,351	2,290	t*	7.9 (21,22)
22	30,319	2,886	t*	
1'	131,852			
2'	131,797	7,053	d	2.2 (2',6')
3'	118,815			
4'	154,384			
5'	115,308	6,778	d	8.1 (5',6')
6'	129,677	7,016	dd	
7'	52,275	3,993	s	
8'	49,488	3,187	s br	
9'	52,698	3,621	s	
1''	118,715			
2''	154,520			
3''	115,348	6,791	d	8.1 (3'',4'')
4''	129,822	7,055	dd	
5''	131,361			
6''	131,832	7,086	d	2.3 (4'',6'')
7''	52,291	4,021	s	
8''	49,606	3,188	s br	
9''	52,732	3,646	s	
10''	29,457	2,703	t*	7.8 (10'',11'')
11''	35,512	2,457	t*	
1-COOH	173,671	12,3	v br	
3-COOH	174,102	12,3	v br	
7-COOH	174,472	12,3	v br	
9-COOH	170,266	12,3	v br	
9'-COOH	170,165	12,3	v br	
11'-COOH	173,779	12,3	v br	

Numbering scheme is that used for MS-III-72. multiplicity: "br" for NH means broadened by slow exchange with residual H2O; for DOTA residual broadening is in fast-exchange regime for conformational equilibria

*C = exchange coalescence with residual H2O

J(H,H) NR = multiplet not well-resolved, either due to linebroadening or overlap with other signals
J couplings listed were determined only from resolved multiplets

13C shifts taken from 2D spectra, no 1D experiment performed at 303K
ND = not detected due to exchange broadening

mult. t* = pseudo triplet for AAB'B' ethyl fragment; ave. vicinal J is given