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SUPPLEMENTARY MATERIAL TO

4-[(4-Acetylphenyl)amino]-2-methylidene-4-oxobutanoic acid, a newly synthesized amide with hydrophilic and hydrophobic segments: Spectroscopic characterization and investigation of its reactive properties

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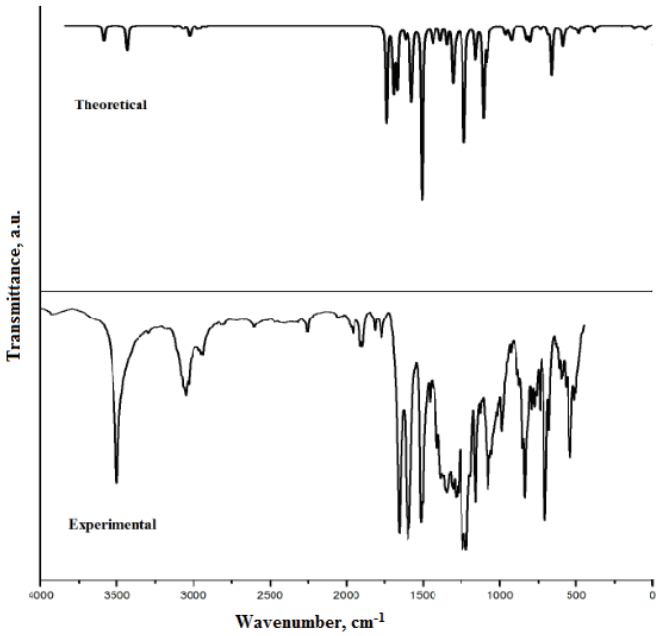


Fig. S-1. The experimental and simulated FT-IR spectra of 4-[(4-acetylphenyl)amino]-2-methylidene-4-oxobutanoic acid.

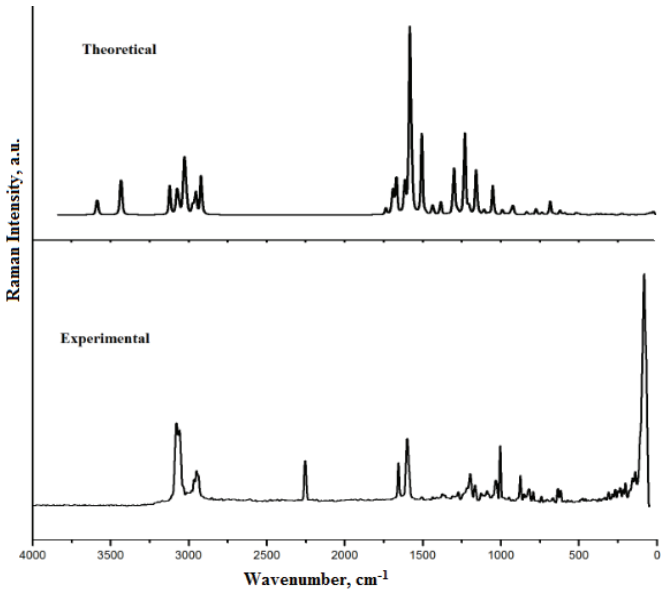
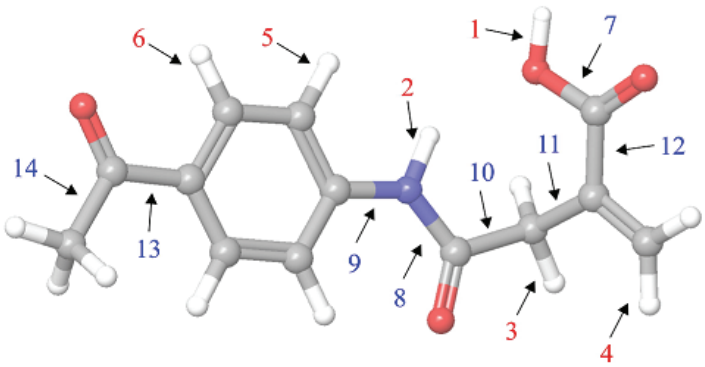


Fig. S-2. The experimental and simulated FT-Raman spectrum of 4-[(4-acetylphenyl)amino]--2-methylidene-4-oxobutanoic acid.



Bond	BDE, kcal mol^{-1}
1	110.23
2	104.58
3	87.23
4	118.62
5	117.09
6	119.45
7	111.20
8	83.13
9	111.28
10	68.74
11	93.73
12	99.36
13	95.61
14	82.58

Fig. S-3. BDE values of all single acyclic bonds of 4-[(4-acetylphenyl)amino]-2-methylidene--4-oxobutanoic acid.

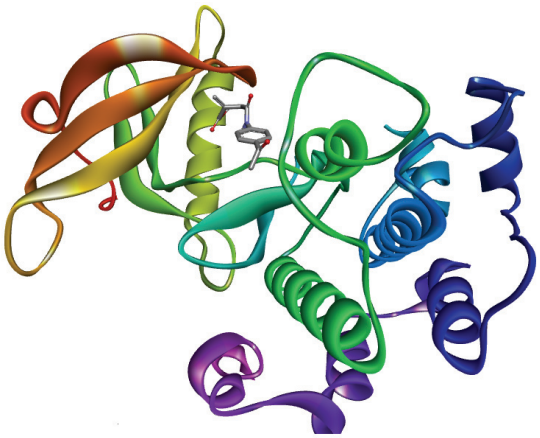


Fig. S-4. The docked ligand inserted in the active site of Insulin Receptor Kinase (IRK).

TABLE S-I. Optimized geometrical parameters of the title compound with XRD data

Bond lengths, Å (DFT/XRD)			
C8–O1	1.2164/1.2222	C13–O2	1.2043/1.2492
O3–H4	0.9699/0.9750	C13–O3	1.3720/1.2882
C27–O5	1.2186/1.2162	N6–H7	1.0120/0.8800
C8–N6	1.3756/1.3542	C17–N6	1.4056/1.4202
C8–C9	1.5388 /1.5232	C9–H10	1.0891/0.9900
C9–H11	1.0923/0.9900	C9–C12	1.5162/1.5042
C12–C13	1.4922/1.4852	C12–C14	1.3369/1.3282
C14–H15	1.0843/0.9820	C14–H16	1.0835/1.0030
C17–C18	1.4068/1.3892	C17–C25	1.4012 /1.3952
C18–H19	1.0868 /0.9500	C18–C20	1.3822 /1.3802
C20–H21	1.0838/0.9500	C20–C22	1.4033/1.3972
C22–C23	1.3999/1.3922	C22–C27	1.4944/1.4972

TABLE S-I. Continued

Bond lengths, Å (DFT/XRD)			
C23–H24	1.0843/0.9500	C23–C25	1.3914/1.3852
C25–H26	1.0792/0.9500	C27–C28	1.5182/1.5042
C28–H29	1.0941/0.9800	C28–H30	1.0941/0.9800
C28–H31	1.0888/0.9800		
Bond angles, ° (DFT/XRD)			
H4–O3–C13	107.1/118.2	H7–N6–C8	115.3/116.8
H7–N6–C17	115.6/116.8	C8–N6–C17	129.0/126.5
O1–C8–N6	124.7/123.5	O1–C8–C9	121.2/121.4
N6–C8–C9	114.1/115.0	C8–C9–H10	105.5/109.4
C8–C9–H11	110.2/109.4	C8–C9–C12	113.3/111.3
H10–C9–H11	107.9/ 108.0	H10–C9–C12	109.2/109.4
H11–C9–C12	110.5/109.4	C9–C12–C13	120.4/116.8
C9–C12–C14	122.6 /123.9	C13–C12–C14	117.1/119.2
O2–C13–O3	121.1/123.3	O2–C13–C12	126.5/120.9
O3–C13–C12	112.3/115.7	C12–C14–H15	121.3/118.9
C12–C14–H16	120.8/122.5	H15–C14–H16	117.9 /118.5
N6–C17–C18	117.1/117.6	N6–C17–C25	123.7/122.6
C18–C17–C25	119.2 /119.6	C17–C18–H19	119.6/ 120.0
C17–C18–C20	120.7/120.0	H19–C18–C20	119.7 /120.0
C18–C20–H21	120.6 /119.4	C18–C20–C22	120.8 /121.1
H21–C20–C22	118.6/119.4	C20–C22–C23	118.1/118.1
C20–C22–C27	118.7 /118.7	C23–C22–C27	123.2 /123.1
C22–C23–H24	120.3 /119.3	C22–C23–C25	121.8/121.3
H24–C23–C25	117.9 /119.3	C17–C25–C23	119.4/119.6
C17–C25–H26	119.9/120.2	C23–C25–H26	120.7/120.2
O5–C27–C22	120.8/120.3	O5–C27–C28	120.4/121.3
C22–C27–C28	118.8 /118.3	C27–C28–H29	111.2/109.5
C27–C28–H30	111.3/109.5	C27–C28–H31	108.9/109.5
H29–C28–H30	107.3/109.5	H29–C28–H31	109.1/109.5
H30–C28–H31	109.1/109.5		
Dihedral angles, ° DFT/XRD			
C17–N6–C8–O1	1.0/–5.0	C17–N6–C8–C9	–178.8/–174.0
C8–N6–C17–C18	178.5/148.4	C8–N6–C17–C25	–1.7/–34.2
O1–C8–C9–C12	–101.7/–35.3	N6–C8–C9–C12	78.1/145.7
C8–C9–C12–C13	–88.6/–68.8	C8–C9–C12–C14	91.6/ 111.3
C9–C12–C13–O2	–176.0/–177.0	C9–C12–C13–O3	3.6/–3.0
C14–C12–C13–O2	3.8/–3.1	C14–C12–C13–O3	–176.6/–176.9
N6–C17–C18–C20	179.9/177.5	C25–C17–C18–C20	0.1/0.0
N6–C17–C25–C23	–179.9/–177.5	C18–C17–C25–C23	–0.1/–0.1
C17–C18–C20–C22	–0.0/0.0	C18–C20–C22–C23	–0.0/0.1
C18–C20–C22–C27	179.9/179.3	C20–C22–C23–C25	0.0/–0.2
C27–C22–C23–C25	–179.9/–179.2	C20–C22–C27–O5	0.2/0.6
C20–C22–C27–C28	–179.8/–179.8	C23–C22–C27–O5	–179.9/–178.8
C23–C22–C27–C28	0.2/0.4	C22–C23–C25–C17	0.0/ 0.2

TABLE S-II. Calculated (scaled) wavenumbers, observed IR, Raman bands and vibrational assignments of the title compound

B3LYP/6-311++G(d) (5D, 7F)			IR	Raman	Assignment[a]
ν / cm^{-1}	IR_I	R_A	ν / cm^{-1}	ν /cm^{-1}	
3587	64.56	89.25	3564	–	νOH(100)
3434	109.55	206.49	3297	–	νNH(98)
3122	2.49	46.33	–	–	νCH(98)
3121	0.41	60.90	–	–	νCH_2(100)
3078	3.18	79.24	3075	3079	νCH(97)
3066	8.29	67.72	3064	3062	νCH(98)
3033	3.02	93.81	–	–	νCH_2(98)
3031	18.36	76.99	–	303	νCH(97)
3024	17.50	114.53	3025	–	νCH_3(99)
3012	4.01	51.44	3008	3009	νCH_2(99)
2974	10.44	42.85	2972	2970	νCH_3(100)
2956	7.94	99.41	2954	2950	νCH_2(99)
2920	3.68	161.22	2928	2930	νCH_3(100)
1737	298.26	16.87	1744	–	νC=O(75)
1694	228.66	72.25	1695	–	νC=O(72)
1672	248.51	123.30	1665	1661	νC=O(78)
1617	39.39	93.90	1610	1600	νC=C(65), δOH(15)
1586	56.67	471.00	1590	–	νPh(60), δNH(10)
1574	283.25	191.24	1580	–	νPh(47), δNH(22)
1508	532.16	199.86	1505	1506	νPh(41), δNH(24)
1483	2.23	3.21	–	–	νPh(30), δNH(48)
1440	35.98	11.78	–	1438	δCH_2(91)
1440	12.31	10.45	–	1438	δCH_3(94)
1431	19.60	5.29	1433	–	δCH_3(90)
1389	47.41	3.94	–	–	νPh(57), δCH_2(14)
1386	10.63	32.59	1383	1381	δCH_2(58), νPh(10)
1346	52.41	1.75	1345	1355	δCH_3(94)
1308	132.82	26.16	–	1308	δOH(41), νCC(24)
1300	71.32	94.23	1302	–	νPh(56), δCH(22)
1288	23.56	7.36	1285	–	νPh(17), δCH(68)
1277	3.01	5.69	1273	1274	δCH_2(85)
1238	6.43	12.83	1240	–	δCH_2(35), δNH(45)
1234	241.44	42.46	–	–	νCO(46), νCN(40)
1231	159.86	153.86	1225	–	νCN(47), νPh(22)
1205	5.92	21.57	1198	1198	νCC(42), δCH_2(15)
1159	121.53	128.73	1157	1162	δCH(68)
1110	246.32	12.17	1112	1115	νCN(11), δCH_2(47)
1105	101.86	0.97	–	–	δCH_2(41), δCH(40)
1082	116.72	4.15	1090	1084	νCC(48), δCH_2(10)
1052	2.09	69.75	1050	–	δCH_3(55), νPhI(25)
1011	0.89	0.29	1013	1008	δCH_3(70), δCH(19)
990	0.80	12.19	988	–	δCH(53), νPhI(34)
965	34.88	4.10	964	–	γOH(95)
943	1.34	0.20	945	946	γCHI(53), τPhI(29)

TABLE S-II. Continued

B3LYP/6-311++G(d) (5D, 7F)			IR	Raman	Assignment[a]
ν / cm^{-1}	IR_I	R_A	ν / cm^{-1}	ν / cm^{-1}	
941	0.23	0.17	–	–	γCHI(73), τPhI(14)
940	11.51	4.15	–	–	νCC(43), δCH$_2$(23)
932	18.42	4.66	–	–	δCH$_2$(44), νCC(10)
924	34.87	19.37	927	921	νCC(35), δCH$_3$(22), δCH$_2$(21)
911	6.59	2.12	–	–	δCH$_2$(39), νCC(19)
835	4.98	8.70	836	–	νPh(43), δC=O(14)
826	48.32	0.29	–	824	γCHI(71), γCN(10), τPhI(10)
807	34.36	0.50	810	–	γCHI(66)
801	21.74	2.30	798	798	γC=O(40), τCH$_2$(18), γCHI(15)
775	2.47	14.08	774	–	γC=O(17), δCH$_2$(26), νCC(10)
739	8.24	4.58	739	739	νCC(48), δCO(10), δPhI(10)
719	0.18	1.22	721	–	τPhI(66), γCN(14), γCC(11)
685	19.02	28.63	–	–	δCC(24), γC=O(40)
661	81.02	1.00	670	664	γNH(49), τC=O(29)
659	80.06	2.12	–	–	τCH$_2$(25), τOH(24), γC=O(13), γNH(13)
624	0.08	8.62	625	–	δPhI(75)
613	5.21	2.71	613	615	τOH(34), δC=O(37)
591	60.07	3.71	589	593	τOH(22), δC=O(20), τCH$_2$(10), δCC(12)
579	12.59	0.46	–	572	γC=O(37), δCH$_3$(13),γCC(10), γCN(10), τPhI(13)
558	7.08	1.86	552	–	γNH(30), τPhI(13)
519	7.37	5.96	517	–	δC=O(35), δCC(17)
501	7.96	2.37	501	–	δCO(31), γCN(10), δCC(10)
484	20.07	0.38	–	480	τPhI(34), δCC(13), δC=O(10)
458	7.05	0.55	464	458	δCC(40), δC=O(10)
411	1.24	1.09	–	–	δCC(36), τCC(11), δC=O(19)
404	0.05	0.08	–	–	τPhI(91)
386	19.05	2.33	–	–	γCC(22), δCN(11), γC=O(11)
361	4.53	1.89	–	367	δCC(44), δC=O(13)
331	0.48	1.60	–	331	δCN(28), δC=O(18), δCC(20)
294	0.59	1.32	–	–	τPhI(29), γCC(27)
284	0.21	0.59	–	282	δCC(16), γCC(11), δCO(10), τPhI(10)
226	0.96	3.57	–	230	δNH(26), δCC(28), δPhI(19)
204	1.26	0.84	–	202	δCC(53), δC=O(17)
163	0.07	0.18	–	168	τCH$_3$(90)
154	0.40	0.61	–	–	δCH$_2$(18), γNH(13), γCC(21), τC=O(11)
120	9.26	0.28	–	–	τCC(31), δCC(18), δCN(17), δNH(10)
103	2.78	0.77	–	–	δCH$_2$(30), τCC(16), τC=O(10)
72	2.19	1.28	–	75	τC=O(49), τCH$_2$(11)
64	1.84	1.19	–	–	τC=O(59), τNH(10)
54	6.72	0.47	–	–	τCH$_2$(37), τNH((21), τC=O(14)
46	4.16	3.23	–	–	τCC(54), τC=O(33)
28	0.17	3.34	–	–	τC=O(40), τNH(22)
23	0.32	3.84	–	–	τCH$_2$(38), τPh(31)

[a]ν: stretching; δ: in-plane deformation; γ: out-of-plane deformation; τ: torsion; Ph: phenyl ring; potential energy distribution (%) is given in brackets in the assignment column; IR_I: IR intensity; R_A: Raman activity

TABLE S-III. Second order perturbation theory analysis of Fock matrix in NBO basis corresponding to the intramolecular bonds of the title compound

Donor(i)	Type	*ED*/e	Acceptor (j)	Type	*ED*/e	$E(2)^a$	$E(i)–E(j)^b$	$F(i,j)^c$
O1–C8	π	1.98727	C9–C12	σ*	0.02577	1.62	0.76	0.031
O2–C13	σ	1.99679	C9–C12	σ*	0.02577	1.02	1.50	0.035
–	–	–	C12–C13	σ*	0.07375	1.70	1.52	0.046
–	π	1.98705	C12–C14	π*	0.04522	3.72	0.43	0.036
O3–C13	σ	1.99593	C12–C14	σ*	0.01274	1.42	1.57	0.042
N6–C8	σ	1.98983	N6–C17	σ*	0.02954	1.96	1.26	0.045
–	–	–	C17–C18	σ*	0.02094	1.53	1.38	0.041
C8–C9	σ	1.97042	N6–C17	σ*	0.02954	4.49	1.06	0.062
–	–	–	C12–C14	π*	0.04522	2.69	0.66	0.038
C12–C13	σ	1.97498	O2–C13	σ*	0.01831	1.02	1.29	0.032
–	–	–	C12–C14	σ*	0.01274	1.85	1.33	0.044
C17–C25	σ	1.97418	N6–C17	σ*	0.02954	1.31	1.13	0.034
–	–	–	C17–C18	σ*	0.02094	3.72	1.25	0.061
–	–	–	C23–C25	σ*	0.01459	2.40	1.29	0.050
C22–C27	σ	1.98068	C18–C20	σ*	0.01261	2.25	1.25	0.047
–	–	–	C20–C22	σ*	0.02187	1.96	1.22	0.044
–	–	–	C22–C23	σ*	0.02298	2.29	1.23	0.047
–	–	–	C23–C25	σ*	0.01459	2.07	1.24	0.045
C27–C28	σ	1.99071	C20–C22	σ*	0.02187	2.35	1.20	0.048
LP O1	σ	1.97381	N6–C8	σ*	0.07744	2.30	1.13	0.046
–	–	–	C8–C9	σ*	0.06928	1.91	1.03	0.040
LP O1	π	1.85987	N6–C8	σ*	0.07744	26.63	0.71	0.124
–	–	–	C8–C9	σ*	0.06928	21.51	0.61	0.104
LP O2	σ	1.97599	O3–C13	σ*	0.11051	1.20	1.01	0.032
–	–	–	C12–C13	σ*	0.07375	2.88	1.10	0.051
LP O2	π	1.83353	O3–C13	σ*	0.11051	36.97	0.59	0.133
–	–	–	C12–C13	σ*	0.07375	19.40	0.68	0.105
LP O3	σ	1.96940	O2–C13	σ*	0.01831	6.36	1.24	0.079
LP O3	π	1.83540	O2–C13	π*	0.23906	40.87	0.35	0.109
LP O5	σ	1.97772	C22–C27	σ*	0.06682	2.05	1.12	0.043
–	–	–	C27–C28	σ*	0.05316	1.49	1.07	0.036
LP O5	π	1.89069	C22–C27	σ*	0.06682	19.90	0.70	0.106
–	–	–	C27–C28	σ*	0.05316	20.48	0.64	0.104
LP N6	σ	1.65329	O1–C8	π*	0.26733	60.78	0.28	0.118
–	–	–	C17–C25	π*	0.37737	36.48	0.30	0.094

[a] $E(2)$ means energy of hyper-conjugative interactions (stabilization energy in kJ mol^{-1}); [b] Energy difference (a.u.) between donor and acceptor i and j NBO orbitals; [c] $F(i,j)$ is the Fock matrix elements (a.u.) between i and j NBO orbitals

TABLE S-IV. NBO results showing the formation of Lewis and non-Lewis orbitals

Bond (A–B)	*ED* / e[a]	*EDA* / %	*EDB* / %	*NBO*	*s* / %	*p* / %
π O1–C8	1.98727	69.04	30.96	$0.8309(sp^{1.00})O$	0.01	99.99
–	–0.37501	–	–	$+0.5564(sp^{1.00})C$	0.01	99.99
σ O2–C13	1.99679	65.83	34.17	$0.8114(sp^{1.35})O$	42.30	57.70
–	–1.11704	–	–	$+0.5845(sp^{1.95})C$	33.90	66.10
πO2–C13	1.98705	69.09	30.91	$0.8312(sp^{99.99})O$	0.06	99.94
–	–0.40395	–	–	$+0.5560(sp^{99.99})C$	0.05	99.95
σO3–C13	1.99593	69.34	30.66	$0.8327(sp^{1.95})O$	33.83	66.17
–	–0.93837	–	–	$+0.5537(sp^{2.82})C$	26.14	73.86
σN6–C8	1.98983	63.40	36.60	$0.7962(sp^{1.77})N$	36.08	36.08
–	–0.83404	–	–	$+0.6050(sp^{2.14})C$	31.81	68.19
σC8–C9	1.97042	48.03	51.97	$0.6930(sp^{1.83})C$	35.36	64.66
–	–0.63420	–	–	$+0.7209(sp^{2.98})C$	25.10	75.90
σC12–C13	1.97498	51.68	48.32	$0.7189(sp^{2.42})C$	29.21	70.89
–	–0.69404	–	–	$+0.6951(sp^{1.50})C$	39.90	60.10
σC17–C25	1.97418	51.50	48.50	$0.7176(sp^{1.70})C$	37.04	62.96
–	–0.70144	–	–	$+0.6964(sp^{2.00})C$	33.33	66.67
σC22–C27	1.98068	52.58	47.42	$0.7251(sp^{2.18})C$	31.42	68.58
–	–0.64905	–	–	$+0.6886(sp^{1.84})C$	35.15	64.85
σC27–C28	1.99071	48.58	51.42	$0.6970(sp^{1.90})C$	34.51	65.49
–	–0.62679	–	–	$+0.7171(sp^{2.70})C$	27.04	72.96
n1 O1	1.97381	–	–	$sp^{0.73}$	57.74	42.26
–	–0.68016	–	–	–	–	–
n2 O1	1.85987	–	–	$sp^{99.99}$	0.02	99.98
–	–0.25478	–	–	–	–	–
n1 O2	1.97599	–	–	$sp^{0.74}$	57.60	42.40
–	–0.70320	–	–	–	–	–
n2 O2	1.83353	–	–	$sp^{1.00}$	0.00	100.00
–	–0.27969	–	–	–	–	–
n1 O3	1.96940	–	–	$sp^{1.27}$	44.08	55.92
–	–0.64024	–	–	–	–	–
n2 O3	1.83540	–	–	$sp^{99.99}$	0.06	99.94
–	–0.36214	–	–	–	–	–
–n1 O5	1.97772	–	–	$sp^{0.76}$	56.80	43.20
–	–0.66999	–	–	–	–	–
–n2 O5	1.89069	–	–	$sp^{99.99}$	0.02	99.98
–	–0.24789	–	–	–	–	–
n1 N6	1.65329	–	–	$sp^{99.99}$	0.06	99.94
–	–0.26843	–	–	–	–	–

[a]*ED* / e is expressed in a.u.

TABLE S-V. Binding affinity of different poses of the title compound as predicted by Autodock Vina

Mode	Affinity, kcal mol^{-1}	Distance from best mode	
		RMSD l.b.	*RMSD* u.b.
1	–10.2	0.000	0.000
2	–10.0	2.008	8.346
3	–9.9	2.373	4.794
4	–9.5	2.236	5.186
5	–9.0	2.376	3.548
6	–8.4	12.047	14.496
7	–8.1	4.790	8.273
8	–7.6	2.719	9.762
8	–7.5	3.384	8.217