

# Microsolvated complexes of ibuprofen as revealed by high-resolution rotational spectroscopy.

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## Abstract:

Hydrogen-bonded complexes between ibuprofen and water generated in a supersonic expansion were characterized by chirped-pulse Fourier transform microwave spectroscopy in the 2-8 GHz frequency range. Four spectra were observed allowing to determine their rotational parameters. Comparison with quantum-chemical calculations led to their identification as the lowest energy 1:1 ibuprofen – water complexes. These correspond to the complexes between water and the four different conformers of ibuprofen previously detected in the gas phase, owing to their similar stabilization energies and abundances. Water seems to not change the conformational distribution of ibuprofen.

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Figure S1. Detected conformers of ibuprofen [ref. 15] showing the inertial axis. The experimentally determined parameters are given in Table S1.

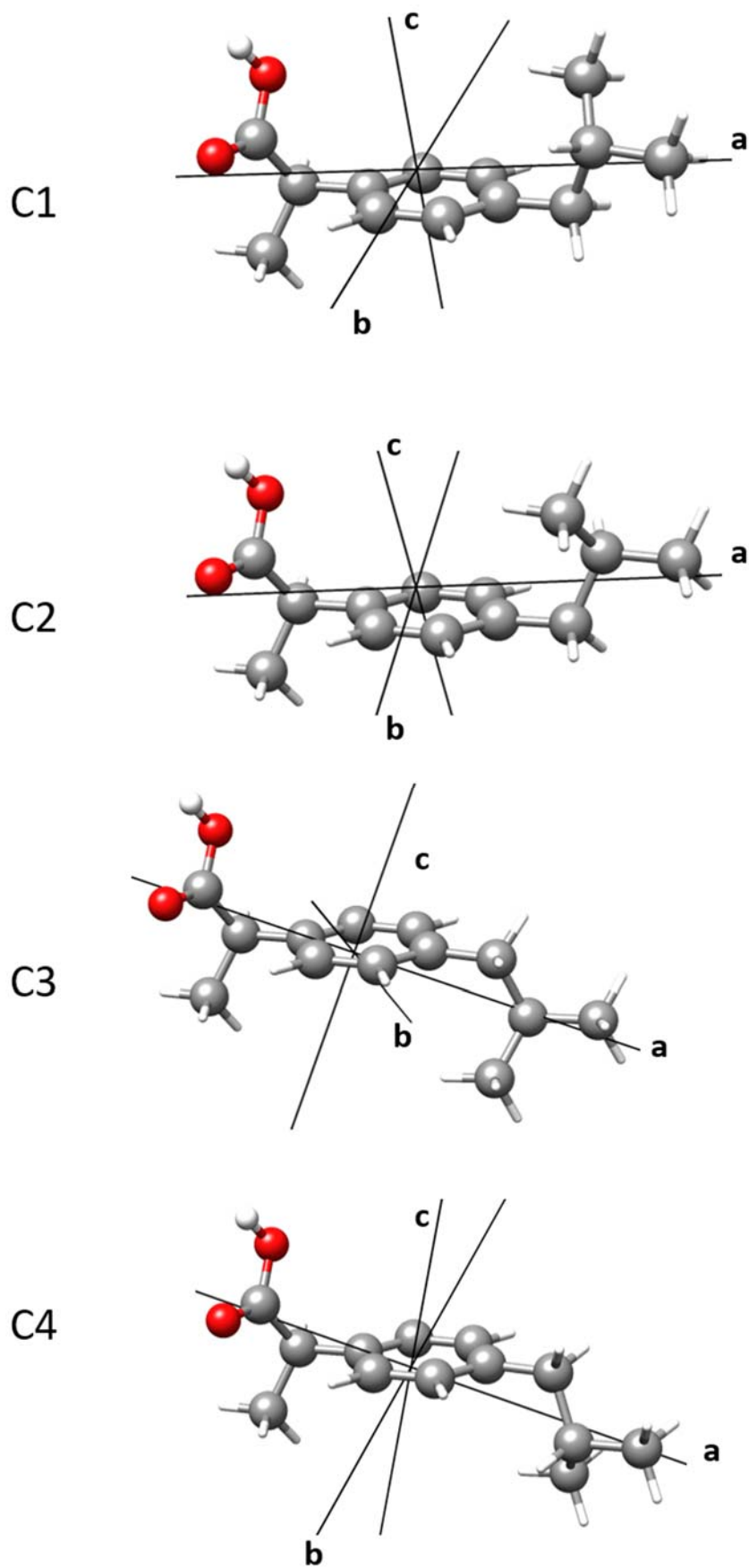


Figure S2. Most stable conformers predicted at the B3LYP-D3/aug-cc-pVDZ level of theory for 1:1 ibuprofen – water complexes showing the inertial axis. The corresponding parameters are given in Table S2.

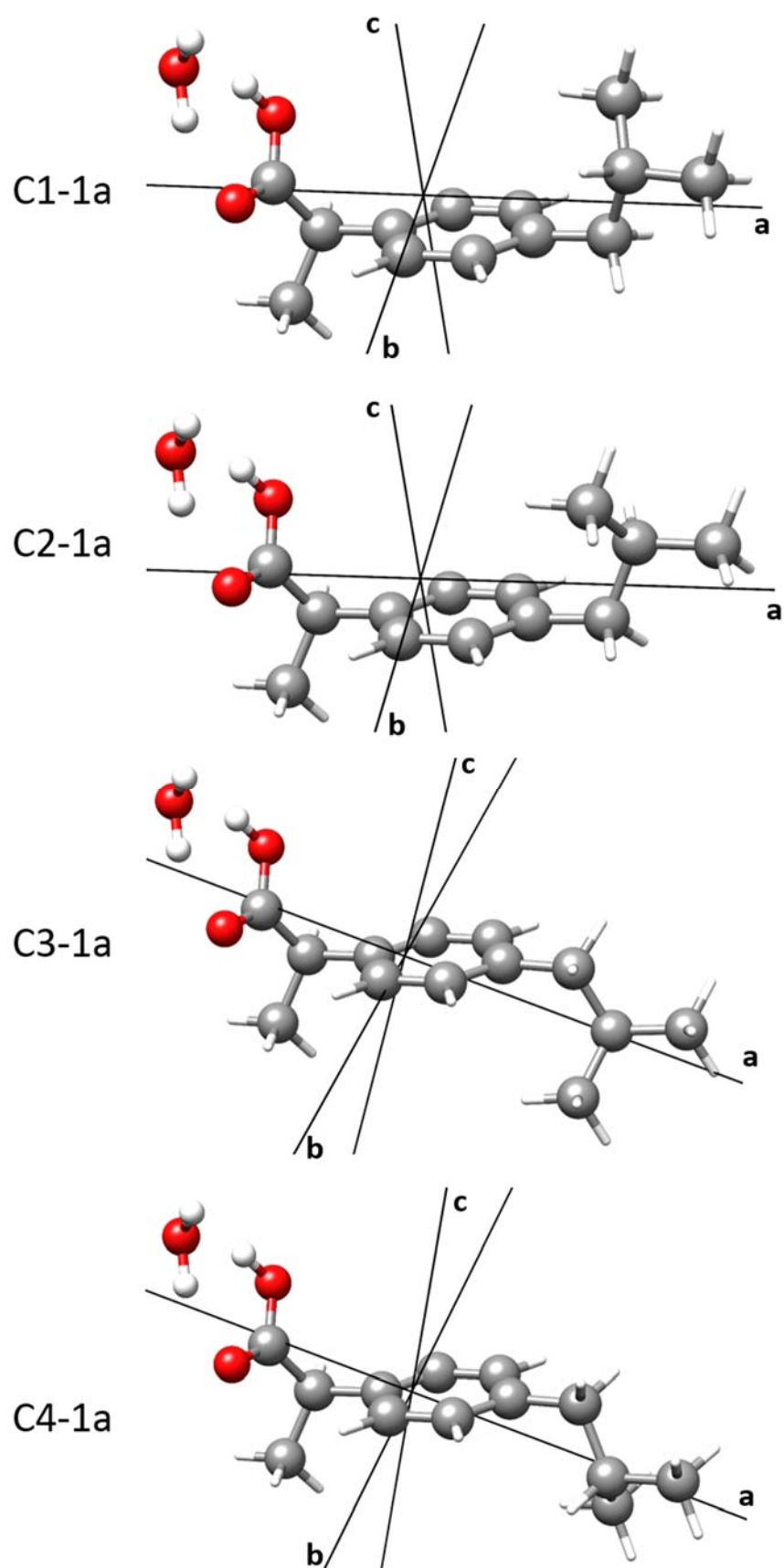


Figure S3. Ibuprofen – water complex C1-1a predicted at the B3LYP-D3/aug-cc-pVDZ level of theory showing the atom labeling.

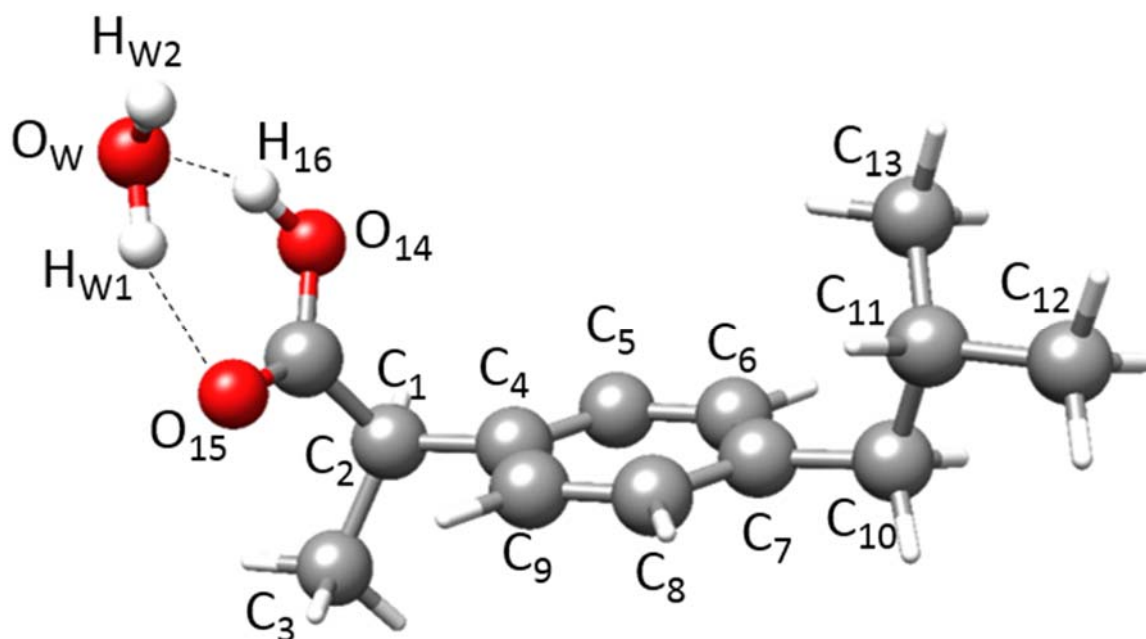


Figure S4. Additional stable conformers predicted at the B3LYP-D3/aug-cc-pVDZ level of theory for 1:1 ibuprofen – water complexes showing the inertial axis. The corresponding parameters are given in Table S2.

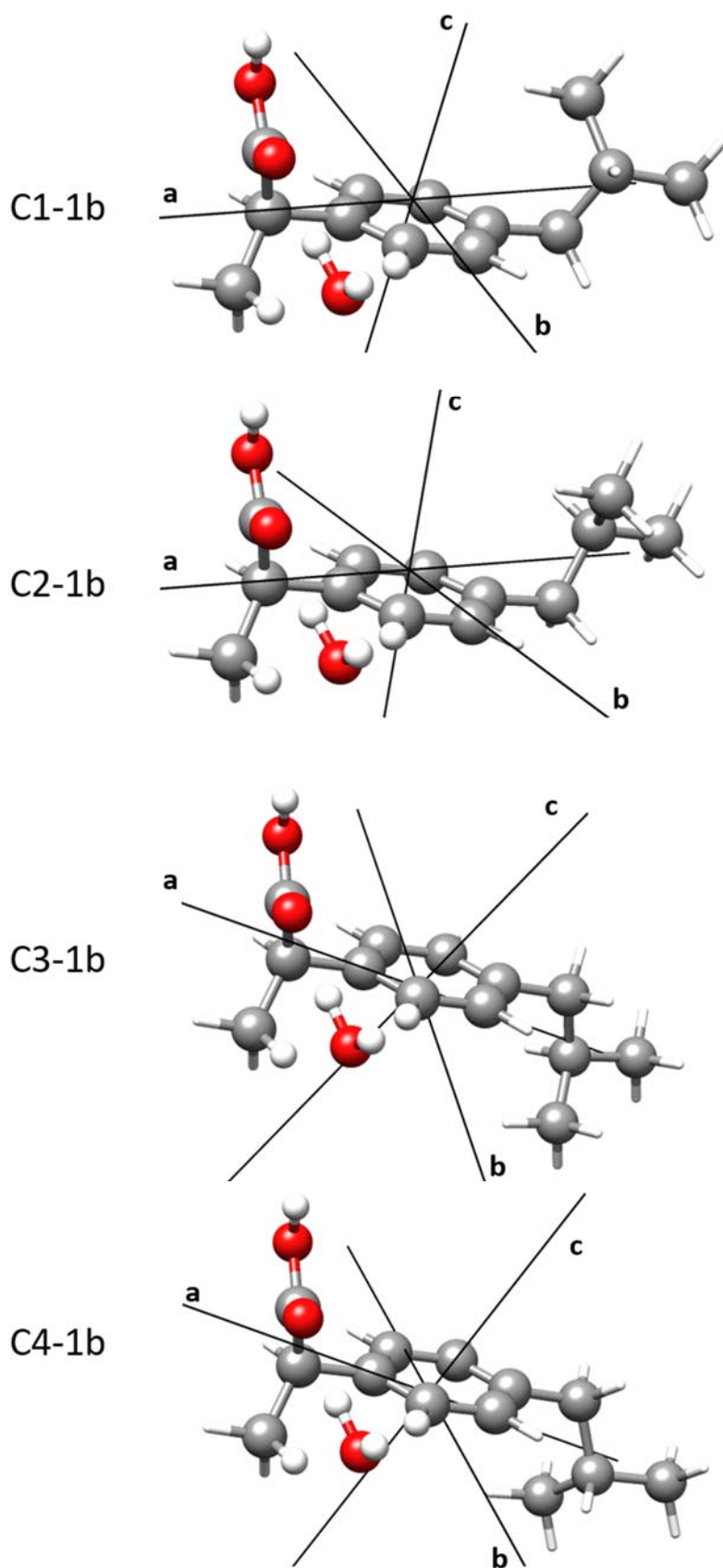
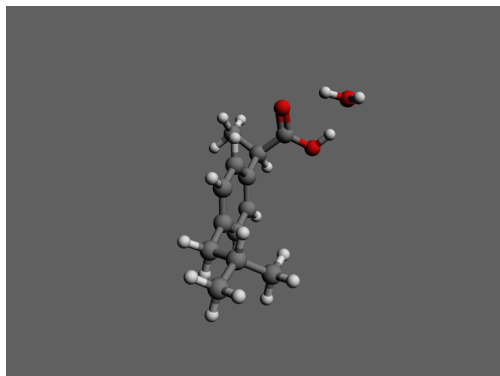
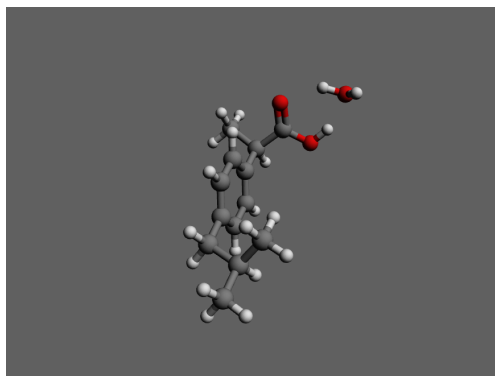


Figure S5. 3D model for the predicted structures for 1:1 ibuprofen – water complexes.

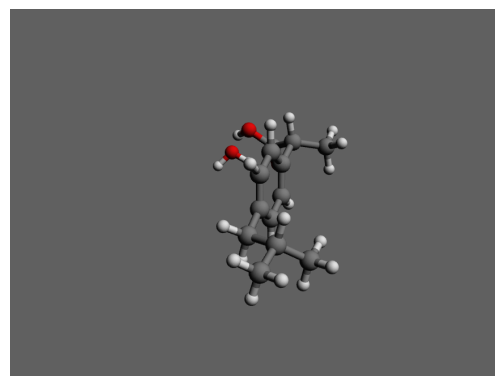
C1-1a



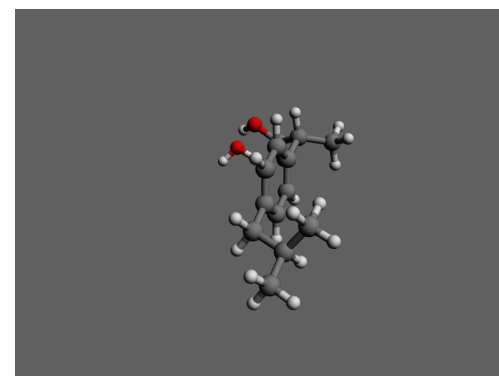
C2-1a



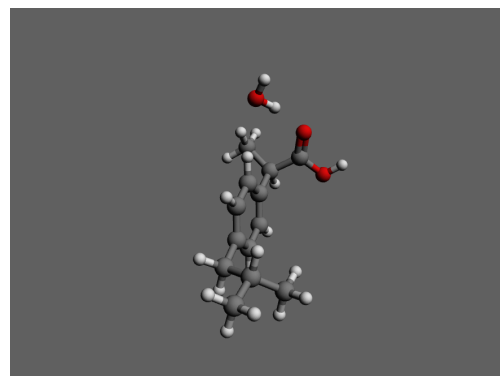
C3-1a



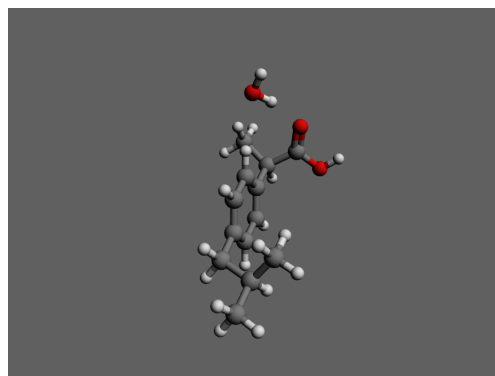
C4-1a



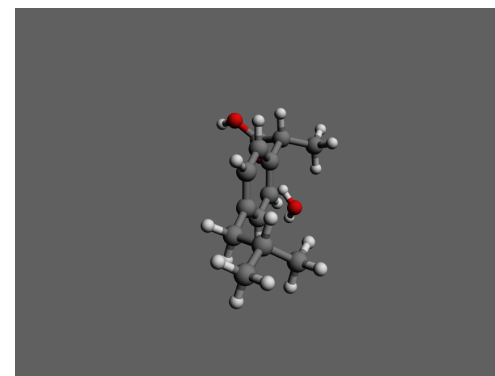
C1-1b



C2-1b



C3-1b



C4-1b

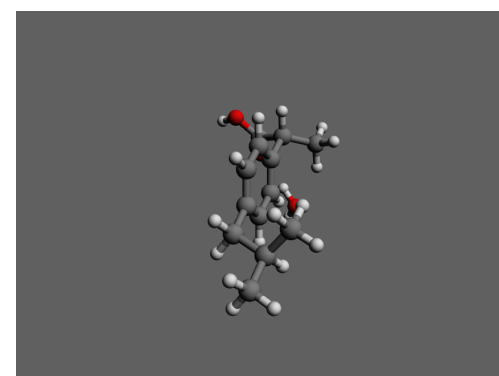


Table S1. Experimental rotational parameters for the ibuprofen monomers previously reported [ref. 15].

Fitted Parameters <sup>a</sup>	C1	C2	C3	C4
<i>A</i> /MHz	1325.656(3) <sup>b</sup>	1357.716(3)	1570.534(4)	1534.787(5)
<i>B</i> /MHz	260.7159(5)	261.4567(4)	245.4447(4)	244.8941(6)
<i>C</i> /MHz	251.1813(5)	248.3119(4)	239.7532(5)	242.1034(6)
$\Delta_J$ /kHz	0.89(21)	0.50(20)	0.69(48)	0.85(55)
$\Delta_{JK}$ /kHz	-0.049(14)	-0.068(12)	0.014(22)	0.013(22)
$\Delta_K$ /kHz	0.012(15)	0.012(13)	0.063(13)	0.067(15)
<i>N</i>	139	151	113	109
$\sigma$ /kHz	33	31	29	38
Derived Parameters				
$P_{aa}$ /uÅ <sup>2</sup>	1784.604(5)	1797.984(4)	1922.580(6)	1910.916(7)
$P_{bb}$ /uÅ <sup>2</sup>	227.405(5)	237.275(4)	185.334(6)	176.535(7)
$P_{cc}$ /uÅ <sup>2</sup>	153.824(5)	134.952(4)	136.454(6)	152.748(7)

<sup>a</sup> *A*, *B* and *C* are the rotational constants.  $\Delta_J$ ,  $\Delta_{JK}$  and  $\Delta_K$ , are quartic centrifugal distortion constants. *N* is the number of rotational transitions fitted.  $\sigma$  is the rms deviation of the fit.  $P_{\alpha\alpha}$  ( $\alpha = a, b$  or  $c$ ) are the planar moments of inertia; these are derived from the moments of inertia  $I_\alpha$  as for example  $P_{cc}=(I_a+I_b-I_c)/2$ . <sup>b</sup> Standard errors are given in parentheses in units of the last digit.



Table S2. Quantum-chemical rotational parameters calculated at the B3LYP-D3/aug-cc-pVDZ level of theory for the 1:1 ibuprofen – water complexes.

Parameter <sup>a</sup>	C1-1a	C2-1a	C3-1a	C4-1a	C1-1b	C2-1b	C3-1b	C4-1b
<i>A</i> /MHz	851.9	865.2	1148.3	1135.2	860.9	880.0	966.4	954.5
<i>B</i> /MHz	223.4	225.0	195.1	196.6	232.3	229.5	224.4	223.2
<i>C</i> /MHz	200.0	198.6	188.1	186.8	219.2	219.0	204.4	205.7
$\Delta_J$ /kHz	0.017	0.016	0.006	0.006	0.009	0.010	0.010	0.010
$\Delta_{JK}$ /kHz	-0.070	-0.070	-0.060	-0.071	0.013	0.024	0.016	0.009
$\Delta_K$ /kHz	0.441	0.458	0.936	0.956	0.160	0.150	0.202	0.202
$\delta_J$ /kHz	0.004	0.004	0.001	0.001	0.000	0.000	0.001	0.000
$\delta_K$ /kHz	0.053	0.048	0.006	0.012	0.004	-0.002	0.036	-0.004
$\kappa$	-0.93	-0.92	-0.98	-0.98	-0.96	-0.97	-0.95	-0.95
$P_{aa}$ /uÅ <sup>2</sup>	2101.2	2103.3	2418.5	2415.4	1947.0	1967.7	2100.8	2095.8
$P_{bb}$ /uÅ <sup>2</sup>	428.2	441.3	268.2	290.0	358.5	339.9	371.6	361.0
$P_{cc}$ /uÅ <sup>2</sup>	164.2	142.8	171.8	155.2	228.5	234.3	151.3	168.4
$\mu_a$ /D	-1.9	-1.9	-1.9	-1.8	0.5	0.6	0.1	0.1
$\mu_b$ /D	-0.2	-0.2	0.5	0.6	1.7	1.6	-1.9	-1.6
$\mu_c$ /D	0.2	0.0	0.1	0.0	1.1	1.4	-0.5	-0.9
$\Delta E$ /cm <sup>-1</sup>	0	27	32	9	1165	1175	1146	1167
$\Delta E$ /kJmol <sup>-1</sup>	0	0	0	0	14	14	14	14
$D_e$ /cm <sup>-1</sup>	-4016	-4020	-4018	-4017	-2722	-2708	-2706	-2721
$D_e$ /kJmol <sup>-1</sup>	-48	-48	-48	-48	-33	-32	-32	-32

<sup>a</sup> *A*, *B* and *C* are the rotational constants.  $\Delta_J$ ,  $\Delta_{JK}$ ,  $\Delta_K$ ,  $\delta_J$  and  $\delta_K$  are the quartic centrifugal distortion constants.  $\kappa$  is the asymmetry parameter derived from the rotational constants;  $\kappa = (2B-A-C)/(A-C)$ .  $P_{\alpha\alpha}$  ( $\alpha = a, b$  or  $c$ ) are the planar moments of inertia; these are derived from the moments of inertia  $I_\alpha$  as for example  $P_{cc}=(I_a+I_b-I_c)/2$ .  $\mu_\alpha$  ( $\alpha = a, b$  or  $c$ ) are the electric dipole moment components, 1 D  $\approx 3.33 \cdot 10^{-30}$  C·m.  $\Delta E$  is the energy relative to the most stable complex.  $D_e$  is the dissociation energy calculated using BSSE corrections [27].

Table S3. Quantum-chemical rotational parameters calculated at the MP2/6-311++G(d,p) level of theory for the 1:1 ibuprofen – water complexes.

Parameter <sup>a</sup>	C1-1a	C2-1a	C3-1a	C4-1a	C1-1b	C2-1b	C3-1b	C4-1b
<i>A</i> /MHz	840.8	864.5	1168.3	1135.9	850.2	874.4	964.7	941.7
<i>B</i> /MHz	229.5	228.4	197.0	199.3	237.8	234.4	227.7	228.7
<i>C</i> /MHz	203.6	201.2	189.5	189.7	224.4	223.7	207.8	209.7
$\Delta_J$ /kHz	0.022	0.022	0.007	0.007	0.010	0.010	0.005	0.005
$\Delta_{JK}$ /kHz	-0.088	-0.111	-0.081	-0.081	0.024	0.009	0.038	0.039
$\Delta_K$ /kHz	0.502	0.634	1.150	1.090	0.150	0.202	0.127	0.132
$\delta_J$ /kHz	0.005	0.005	0.001	0.001	0.000	0.000	0.000	0.000
$\delta_K$ /kHz	0.065	0.063	0.014	0.010	-0.002	-0.004	0.026	0.005
$\kappa$	-0.92	-0.92	-0.98	-0.98	-0.96	-0.97	-0.95	-0.95
$P_{aa}$ /uÅ <sup>2</sup>	2041.6	2070.0	2399.8	2377.5	1891.5	1918.6	2063.8	2041.6
$P_{bb}$ /uÅ <sup>2</sup>	440.6	441.9	267.0	286.6	360.7	340.5	368.2	368.4
$P_{cc}$ /uÅ <sup>2</sup>	160.5	142.7	165.5	158.3	233.8	237.4	155.7	168.2
$\mu_a$ /D	-1.4	-1.4	-1.3	-1.3	0.0	0.1	-0.3	-0.4
$\mu_b$ /D	-0.7	-0.7	0.8	1.0	1.2	1.3	-1.5	-1.2
$\mu_c$ /D	0.5	0.3	-0.3	-0.3	1.4	1.5	-0.7	-0.9
$\Delta E$ /cm <sup>-1</sup>	48	0	8	41	1135	1104	1110	1099
$\Delta E$ /kJmol <sup>-1</sup>	1	0	0	0	14	13	13	13
$D_e$ /cm <sup>-1</sup>	-2967	-2971	-2971	-2969	-1910	-1906	-1914	-1919
$D_e$ /kJmol <sup>-1</sup>	-35	-35	-35	-35	-23	-23	-23	-23

<sup>a</sup> *A*, *B* and *C* are the rotational constants.  $\Delta_J$ ,  $\Delta_{JK}$ ,  $\Delta_K$ ,  $\delta_J$  and  $\delta_K$  are the quartic centrifugal distortion constants.  $\kappa$  is the asymmetry parameter derived from the rotational constants;  $\kappa = (2B-A-C)/(A-C)$ .  $P_{\alpha\alpha}$  ( $\alpha = a, b$  or  $c$ ) are the planar moments of inertia; these are derived from the moments of inertia  $I_\alpha$  as for example  $P_{cc}=(I_a+I_b-I_c)/2$ .  $\mu_\alpha$  ( $\alpha = a, b$  or  $c$ ) are the electric dipole moment components, 1 D  $\approx 3.33 \cdot 10^{-30}$  C·m.  $\Delta E$  is the energy relative to the most stable complex.  $D_e$  is the dissociation energy calculated using BSSE corrections [27].

Table S4. Comparison between the hydrogen bond parameters predicted in this work for the 1:1 ibuprofen – water complexes and different acid molecules – water complexes reported.

B3LYP-D3 <sup>a</sup>	C1-1a	C2-1a	C3-1a	C4-1a
$r(\text{O}_W \cdots \text{H}_{16}) / \text{\AA}^b$	1.791	1.790	1.791	1.791
$r(\text{O}_{15} \cdots \text{H}_{W1}) / \text{\AA}$	1.929	1.930	1.930	1.931
$\angle(\text{O}_W - \text{H}_{W1} \cdots \text{O}_{15}) / \text{degree}$	141.0	140.9	141.0	140.9
$\angle(\text{O}_{14} - \text{H}_{16} \cdots \text{O}_W) / \text{degree}$	156.4	156.5	156.5	156.5
$\angle(\text{H}_{W1} \cdots \text{O}_{15} = \text{C}) / \text{degree}$	107.5	107.5	107.5	107.5
$\angle(\text{H}_{16} \cdots \text{O}_W - \text{H}_{W1}) / \text{degree}$	82.9	82.9	82.9	82.9
$\tau(\text{H}_{W2} - \text{O}_W - \text{H}_{W1} \cdots \text{O}_{15}) / \text{degree}$	125.5	125.4	125.3	125.1
MP2 <sup>a</sup>	C1-1a	C2-1a	C3-1a	C4-1a
$r(\text{O}_W \cdots \text{H}_{16}) / \text{\AA}$	1.802	1.803	1.801	1.802
$r(\text{O}_{15} \cdots \text{H}_{W1}) / \text{\AA}$	2.036	2.035	2.035	2.035
$\angle(\text{O}_W - \text{H}_{W1} \cdots \text{O}_{15}) / \text{degree}$	133.3	133.3	133.4	133.4
$\angle(\text{O}_{14} - \text{H}_{16} \cdots \text{O}_W) / \text{degree}$	158.3	158.2	158.3	158.3
$\angle(\text{H}_{W1} \cdots \text{O}_{15} = \text{C}) / \text{degree}$	108.6	108.6	108.6	108.6
$\angle(\text{H}_{16} \cdots \text{O}_W - \text{H}_{W1}) / \text{degree}$	87.8	87.8	87.8	87.8
$\tau(\text{H}_{W2} - \text{O}_W - \text{H}_{W1} \cdots \text{O}_{15}) / \text{degree}$	136.6	136.8	136.5	136.4
Reported <sup>c</sup>	Nitric – water <sup>d</sup>	Form – water <sup>e</sup>	Gly – water <sup>f</sup>	Benz – water <sup>g</sup>
$r(\text{O}_W \cdots \text{H}_{16}) / \text{\AA}$	1.779(33)	1.810	1.806(1)	1.80
$r(\text{O}_{15} \cdots \text{H}_{W1}) / \text{\AA}$	2.3	2.2210	2.073(2)	1.95
$\angle(\text{O}_W - \text{H}_{W1} \cdots \text{O}_{15}) / \text{degree}$	-	120.3	126.4(5)	139.5
$\angle(\text{O}_{14} - \text{H}_{16} \cdots \text{O}_W) / \text{degree}$	174.5(41)	157.7	161.8(1)	157.4
$\angle(\text{H}_{W1} \cdots \text{O}_{15} = \text{C}) / \text{degree}$	-	110.6	112.4(1)	-
$\angle(\text{H}_{16} \cdots \text{O}_W - \text{H}_{W1}) / \text{degree}$	92(8)	97.2	91.4(7)	-
$\tau(\text{H}_{W2} - \text{O}_W - \text{H}_{W1} \cdots \text{O}_{15}) / \text{degree}$	-	-	140.0	-

<sup>a</sup> Optimized geometries at the B3LYP-D3/aug-cc-pVDZ or at the MP2/6-311++G(d,p) level of theory. <sup>b</sup> See Figure S3 for atom labeling. <sup>c</sup> Notation represents the similar atoms of the ibuprofen – water complexes. The use of the same notation scheme denote that we are giving the same hydrogen bond parameters. <sup>d</sup> Values from reference [24a] for the nitric acid – water complex. <sup>e</sup> Values from reference [24b] for the formic acid – water complex. <sup>f</sup> Values from reference [24c] for the glycine – water complex. <sup>g</sup> Values from reference [24d] for the benzoic acid – water complex.

Table S5. a) Calculated rotational constants, moments of inertia and planar moments of inertia for the monomer, and b) those corresponding to the 1a complex assigning zero mass to the water molecule.

a)	B3LYP-D3 <sup>a</sup>	C1	C2	C3	C4
	<i>A</i> /MHz	1314.5	1339.5	1559.9	1531.3
	<i>B</i> /MHz	257.8	259.2	243.6	242.7
	<i>C</i> /MHz	249.2	246.5	238.2	240.2
	<i>I<sub>a</sub></i> /uÅ <sup>2</sup>	384.5	377.3	324.0	330.0
	<i>I<sub>b</sub></i> /uÅ <sup>2</sup>	1959.9	1949.6	2074.4	2082.4
	<i>I<sub>c</sub></i> /uÅ <sup>2</sup>	2027.6	2050.0	2121.7	2103.6
	<i>P<sub>aa</sub></i> /uÅ <sup>2</sup>	1801.5	1811.2	1936.1	1928.0
	<i>P<sub>bb</sub></i> /uÅ <sup>2</sup>	226.1	238.9	185.6	175.6
	<i>P<sub>cc</sub></i> /uÅ <sup>2</sup>	158.4	138.4	138.3	154.4

b)	B3LYP-D3 <sup>a</sup>	C1	C2	C3	C4
	<i>A</i> /MHz	1311.4	1331.6	1558.2	1538.6
	<i>B</i> /MHz	258.7	260.4	244.1	242.2
	<i>C</i> /MHz	250.0	248.2	238.0	239.9
	<i>I<sub>a</sub></i> /uÅ <sup>2</sup>	385.4	379.5	324.3	328.4
	<i>I<sub>b</sub></i> /uÅ <sup>2</sup>	1953.7	1940.9	2070.6	2086.5
	<i>I<sub>c</sub></i> /uÅ <sup>2</sup>	2021.2	2036.5	2123.4	2106.3
	<i>P<sub>aa</sub></i> /uÅ <sup>2</sup>	1794.7	1798.9	1934.8	1932.2
	<i>P<sub>bb</sub></i> /uÅ <sup>2</sup>	226.4	237.5	188.6	174.1
	<i>P<sub>cc</sub></i> /uÅ <sup>2</sup>	158.9	142.0	135.8	154.3

<sup>a</sup> Optimized geometries at the B3LYP-D3/aug-cc-pVDZ level of theory.

Table S6. Observed rotational transitions and residuals (all the values in MHz) for the 1:1 ibuprofen – water complex C1-1a in the ground vibrational state for transitions of the type  $J'K'_{-1}K'_{+1} \leftarrow J''K''_{-1}K''_{+1}$ .

$J'$	$K'_{-1}$	$K'_{+1}$	$J''$	$K''_{-1}$	$K''_{+1}$	Obs.	Obs. - Calc	$J'$	$K'_{-1}$	$K'_{+1}$	$J''$	$K''_{-1}$	$K''_{+1}$	Obs.	Obs. - Calc
5	1	5	4	1	4	2063.4583	-0.0165	10	0	10	9	0	9	4156.8220	0.0021
5	0	5	4	0	4	2113.8883	-0.0044	10	2	9	9	2	8	4237.9689	-0.0006
5	1	4	4	1	3	2186.1456	0.0096	10	4	6	9	4	5	4265.0680	0.0037
6	1	6	5	1	5	2474.3987	-0.0059	10	3	8	9	3	7	4267.0502	-0.0017
6	0	6	5	0	5	2529.2721	-0.0051	10	3	7	9	3	6	4276.8850	-0.0026
6	2	5	5	2	4	2550.3104	0.0073	10	2	8	9	2	7	4336.5940	0.0017
6	2	4	5	2	3	2574.5085	0.0002	10	1	9	9	1	8	4345.1664	-0.0044
6	1	5	5	1	4	2621.2157	0.0101	11	1	11	10	1	10	4515.5408	0.0061
7	1	7	6	1	6	2884.4736	-0.0064	11	0	11	10	0	10	4557.2159	-0.0055
7	0	7	6	0	6	2941.1301	0.0060	11	2	10	10	2	9	4657.3000	-0.0158
7	3	5	6	3	4	2984.2012	0.0043	11	3	9	10	3	8	4694.8442	0.0057
7	3	4	6	3	3	2985.8025	0.0028	11	1	10	10	1	9	4770.2215	-0.0034
7	2	5	6	2	4	3011.4814	0.0056	11	2	9	10	2	8	4780.7760	0.0025
7	1	6	6	1	5	3054.9841	0.0054	12	1	12	11	1	11	4921.0709	0.0040
8	1	8	7	1	7	3293.6370	-0.0055	12	0	12	11	0	11	4956.4039	0.0086
8	0	8	7	0	7	3349.4223	0.0041	12	2	11	11	2	10	5075.4607	0.0064
8	2	7	7	2	6	3395.9790	-0.0139	12	2	10	11	2	9	5224.7295	-0.0020
8	2	6	7	2	5	3451.1528	0.0050	13	0	13	12	0	12	5354.9725	0.0105
8	1	7	7	1	6	3487.1427	0.0019	13	2	12	12	2	11	5492.3116	-0.0059
9	1	9	8	1	8	3701.8600	-0.0054	13	1	12	12	1	11	5610.3340	-0.0102
9	0	9	8	0	8	3754.4646	0.0047								
9	2	8	8	2	7	3817.4963	-0.0010								
9	3	7	8	3	6	3839.2729	-0.0005								
9	3	6	8	3	5	3845.0694	-0.0050								
9	2	7	8	2	6	3893.0883	-0.0026								
9	1	8	8	1	7	3917.3409	0.0048								
10	1	10	9	1	9	4109.1528	0.0003								

Table S7. Observed rotational transitions and residuals (all the values in MHz) for the 1:1 ibuprofen – water complex C2-1a in the ground vibrational state for transitions of the type  $J'K'_{-1}K'_{+1} \leftarrow J''K''_{-1}K''_{+1}$ .

$J'$	$K'_{-1}$	$K'_{+1}$	$J''$	$K''_{-1}$	$K''_{+1}$	Obs.	Obs. - Calc	$J'$	$K'_{-1}$	$K'_{+1}$	$J''$	$K''_{-1}$	$K''_{+1}$	Obs.	Obs. - Calc
5	1	5	4	1	4	2047.1666	-0.0096	9	2	7	8	2	6	3882.7941	-0.0004
5	0	5	4	0	4	2101.5026	0.0011	9	1	8	8	1	7	3905.0030	-0.0073
5	1	4	4	1	3	2180.8406	0.0064	10	0	10	9	0	9	4123.2106	-0.0005
6	0	6	5	0	5	2513.3599	-0.0042	10	2	8	9	2	7	4326.1237	0.0007
6	2	5	5	2	4	2537.4238	0.0021	10	1	9	9	1	8	4330.2788	0.0000
6	4	2	5	4	1	2543.8694	-0.0055	11	1	11	10	1	10	4476.4893	-0.0102
6	4	3	5	4	2	2543.8694	0.0032	11	2	9	10	2	8	4769.9351	-0.0102
6	3	4	5	3	3	2545.1424	-0.0064	12	0	12	11	0	11	4913.3333	0.0198
6	3	3	5	3	2	2546.0067	-0.0059	12	4	9	11	4	8	5098.7178	-0.0027
6	2	4	5	2	3	2565.1438	0.0143	12	3	10	11	3	9	5099.3684	-0.0079
6	1	5	5	1	4	2614.5161	0.0038	12	4	8	11	4	7	5100.2572	-0.0018
7	0	7	6	0	6	2921.2395	-0.0061	12	3	9	11	3	8	5128.1649	0.0061
7	2	6	6	2	5	2958.2705	0.0044								
7	2	5	6	2	4	3001.5911	0.0131								
7	1	6	6	1	5	3046.6887	0.0003								
8	1	8	7	1	7	3266.4673	-0.0046								
8	0	8	7	0	7	3325.1828	-0.0073								
8	2	7	7	2	6	3378.1681	-0.0011								
8	2	6	7	2	5	3440.9921	0.0035								
8	1	7	7	1	6	3476.9920	-0.0014								
9	1	9	8	1	8	3670.8455	0.0040								
9	0	9	8	0	8	3725.6074	-0.0022								
9	2	8	8	2	7	3797.0132	0.0054								
9	4	6	8	4	5	3819.3601	0.0026								
9	4	5	8	4	4	3819.5543	0.0045								
9	3	7	8	3	6	3821.8420	0.0071								
9	3	6	8	3	5	3828.8253	-0.0067								

Table S8. Observed rotational transitions and residuals (all the values in MHz) for the 1:1 ibuprofen – water complex C3-1a in the ground vibrational state for transitions of the type  $J'K'_{-1}K'_{+1} \leftarrow J''K''_{-1}K''_{+1}$ .

$J'$	$K'_{-1}$	$K'_{+1}$	$J''$	$K''_{-1}$	$K''_{+1}$	Obs.	Obs. - Calc	$J'$	$K'_{-1}$	$K'_{+1}$	$J''$	$K''_{-1}$	$K''_{+1}$	Obs.	Obs. - Calc
6	1	6	5	1	5	2279.8126	-0.0017	10	5	6	9	5	5	3838.9739	0.0005
6	0	6	5	0	5	2301.5446	-0.0029	10	5	5	9	5	4	3838.9739	0.0005
6	2	5	5	2	4	2302.9345	-0.0039	10	4	7	9	4	6	3839.1591	0.0080
6	2	4	5	2	3	2304.5321	0.0008	10	4	6	9	4	5	3839.1591	0.0071
6	1	5	5	1	4	2325.7476	0.0086	10	3	8	9	3	7	3839.5194	0.0004
7	0	7	6	0	6	2684.4447	-0.0036	10	3	7	9	3	6	3839.6642	0.0112
7	2	6	6	2	5	2686.6404	-0.0032	10	2	8	9	2	7	3844.8566	0.0018
7	2	5	6	2	4	2689.1888	-0.0009	10	1	9	9	1	8	3874.9434	0.0053
7	1	6	6	1	5	2713.1844	0.0028	11	1	11	10	1	10	4177.9564	0.0002
8	1	8	7	1	7	3039.3336	-0.0019	11	0	11	10	0	10	4212.5018	0.0040
8	0	8	7	0	7	3067.0367	0.0029	11	2	10	10	2	9	4220.8446	0.0007
8	2	7	7	2	6	3070.2934	-0.0011	11	4	7	10	4	6	4223.1753	-0.0025
8	4	5	7	4	4	3071.1775	-0.0062	11	4	8	10	4	7	4223.1754	-0.0006
8	4	4	7	4	3	3071.1775	-0.0064	11	3	9	10	3	8	4223.6491	0.0002
8	3	6	7	3	5	3071.4006	0.0185	11	3	8	10	3	7	4223.8710	0.0044
8	3	5	7	3	4	3071.4006	-0.0241	11	2	9	10	2	8	4230.7371	-0.0037
8	2	6	7	2	5	3074.1067	-0.0013	11	1	10	10	1	9	4261.9548	0.0039
8	1	7	7	1	6	3100.5367	-0.0016	12	1	12	11	1	11	4557.2955	0.0078
9	1	9	8	1	8	3418.9753	0.0027	12	2	11	11	2	10	4604.1925	-0.0076
9	0	9	8	0	8	3449.2551	-0.0071	12	2	10	11	2	9	4616.9928	-0.0070
9	2	8	8	2	7	3453.8778	-0.0056	13	0	13	12	0	12	4973.8898	-0.0071
9	4	5	8	4	4	3455.1519	-0.0031	14	0	14	13	0	13	5353.8536	0.0011
9	4	6	8	4	5	3455.1519	-0.0027	14	1	13	13	1	12	5422.0416	0.0000
9	2	7	8	2	6	3459.3208	0.0013								
9	1	8	8	1	7	3487.7962	0.0008								
10	1	10	9	1	9	3798.5222	0.0069								
10	0	10	9	0	9	3831.0923	-0.0029								

Table S9. Observed rotational transitions and residuals (all the values in MHz) for the 1:1 ibuprofen – water complex C4-1a in the ground vibrational state for transitions of the type  $J'K'_{-1}K'_{+1} \leftarrow J''K''_{-1}K''_{+1}$ .

$J'$	$K'_{-1}$	$K'_{+1}$	$J''$	$K''_{-1}$	$K''_{+1}$	Obs.	Obs. - Calc.	$J'$	$K'_{-1}$	$K'_{+1}$	$J''$	$K''_{-1}$	$K''_{+1}$	Obs.	Obs. - Calc.	$J'$	$K'_{-1}$	$K'_{+1}$	$J''$	$K''_{-1}$	$K''_{+1}$	Obs.	Obs. - Calc.
6	1	6	5	1	5	2283.0417	0.0054	9	3	7	8	3	6	3472.3606	-0.0108	14	0	14	13	0	13	5364.1469	-0.0042
6	0	6	5	0	5	2311.1938	-0.0009	9	3	6	8	3	5	3472.5675	0.0039								
6	2	5	5	2	4	2313.7019	0.0047	9	2	7	8	2	6	3479.3644	0.0003								
6	3	3	5	3	2	2314.5258	-0.0086	9	1	8	8	1	7	3514.1878	-0.0030								
6	3	4	5	3	3	2314.5258	0.0146	10	1	10	9	1	9	3803.0003	0.0042								
6	1	5	5	1	4	2343.7784	0.0003	10	0	10	9	0	9	3843.4117	-0.0040								
7	0	7	6	0	6	2695.1580	0.0015	10	2	9	9	2	8	3854.6869	0.0006								
7	2	6	6	2	5	2699.0983	-0.0051	10	5	5	9	5	4	3857.5023	0.0046								
7	4	3	6	4	2	2700.1613	-0.0016	10	5	6	9	5	5	3857.5026	0.0049								
7	4	4	6	4	3	2700.1613	-0.0013	10	4	6	9	4	5	3857.8272	-0.0018								
7	3	4	6	3	3	2700.4590	0.0028	10	4	7	9	4	6	3857.8272	0.0011								
7	2	5	6	2	4	2703.6873	0.0021	10	3	8	9	3	7	3858.4405	-0.0134								
7	1	6	6	1	5	2734.0811	0.0000	10	3	7	9	3	6	3858.7782	-0.0047								
8	1	8	7	1	7	3043.3115	-0.0007	10	2	8	9	2	7	3868.0193	-0.0036								
8	0	8	7	0	7	3078.5553	-0.0024	10	1	9	9	1	8	3903.9628	0.0204								
8	2	7	7	2	6	3084.4111	-0.0018	11	1	11	10	1	10	4182.5871	0.0041								
8	5	3	7	5	2	3085.8439	0.0024	11	0	11	10	0	10	4224.7603	-0.0048								
8	5	4	7	5	3	3085.8439	0.0024	11	4	7	10	4	6	4243.8159	-0.0023								
8	4	5	7	4	4	3086.0089	0.0024	11	4	8	10	4	7	4243.8159	0.0036								
8	4	4	7	4	3	3086.0089	0.0019	11	3	9	10	3	8	4244.5902	-0.0142								
8	3	6	7	3	5	3086.3545	-0.0012	11	3	8	10	3	7	4245.1370	-0.0013								
8	3	5	7	3	4	3086.4629	0.0023	11	2	9	10	2	8	4257.2767	0.0000								
8	2	6	7	2	5	3091.2667	0.0000	11	1	10	10	1	9	4293.4522	0.0003								
8	1	7	7	1	6	3124.2274	-0.0002	12	1	12	11	1	11	4561.9874	0.0013								
9	1	9	8	1	8	3423.2337	-0.0013	12	0	12	11	0	11	4605.3524	0.0071								
9	0	9	8	0	8	3461.3285	-0.0021	13	1	13	12	1	12	4941.2016	0.0049								
9	2	8	8	2	7	3469.6092	-0.0025	13	2	11	12	2	10	5037.6302	0.0028								