

Supplementary information for:

Hydrogen-Bond-Assisted Conformational Selection of Picaridin in the Gas Phase

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Understanding the intrinsic shape of bioactive molecules such as picaridin is key to elucidating their mode of action. In this work, we characterize the gas-phase conformational landscape of picaridin, a flexible chiral repellent with two stereocenters. Broadband rotational spectroscopy combined with quantum chemical calculations reveals a single dominant conformer per enantiomeric pair, both stabilized by internal O—H...O hydrogen bonds. These intramolecular interactions induce conformational locking, constraining the hydroxyethyl chain and favouring a compact geometry. Non-covalent interaction analysis further confirms that dispersion and hydrogen bonding play a central role in conformational selection under isolated conditions.

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Table S4. Observed transition frequencies for the lowest energy conformer for the picaridin (*S,R/R,S*) diastereomer.

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Figure S1. Predicted (B3LYP-D3(BJ)/def2-TZVP) conformations and relative zero-point corrected energies given in kJ/mol for picaridin (*R,R/S,S*) pair. Black line represents the intramolecular hydrogen bonding.

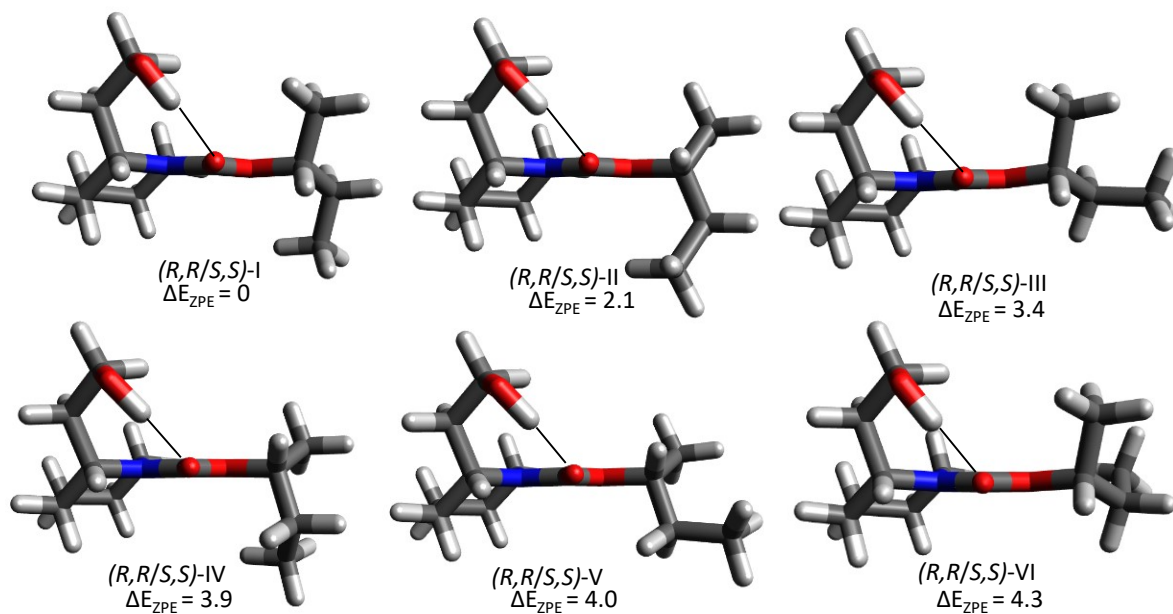


Figure S2. Predicted (B3LYP-D3(BJ)/def2-TZVP) conformations and relative zero-point corrected energies given in kJ/mol for picaridin (*S,R/R,S*) pair. Black line represents the intramolecular hydrogen bonding.

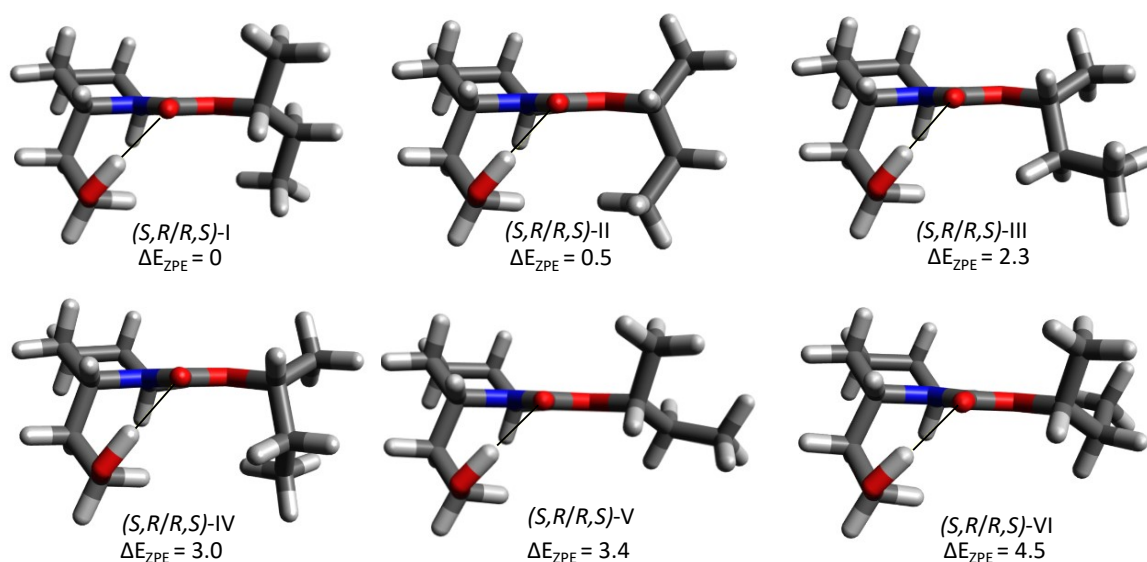


Figure S3. Rotational spectrum of picaridin in the 3-6 GHz range, experimental (upwards) and simulations based on the experimental rotational parameters for the two observed conformers (downwards).

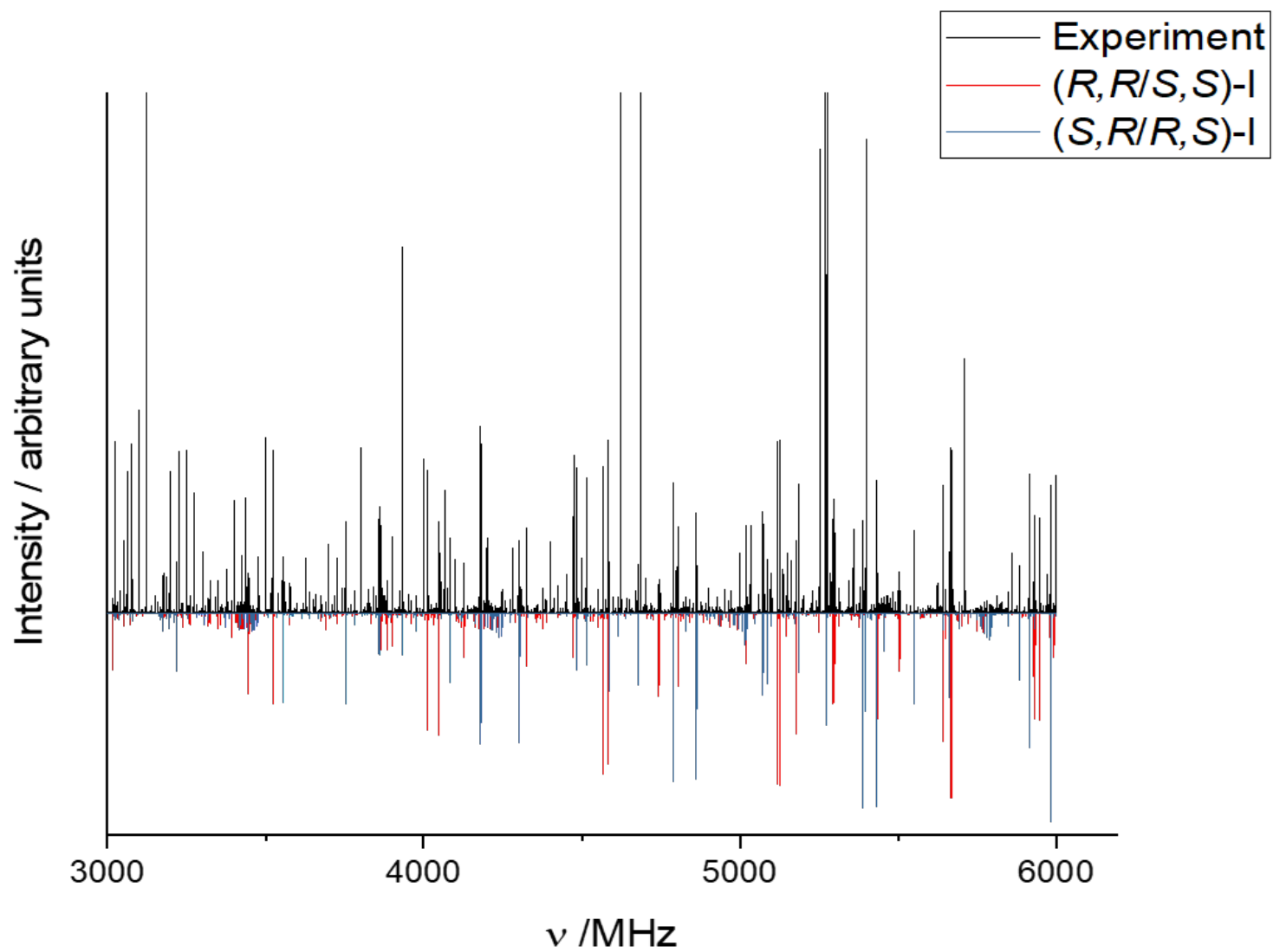


Figure S4. Potential energy scan for conformational relaxation from conformer II to I for both diastereomeric pairs (R,R/S,S and (S,R/R,S) at the B3LYP-D3(BJ)/def2-TZVP level of theory. The graph scans ϕ dihedral angle (C7-O9-C11-C12) in steps of 10 degrees.

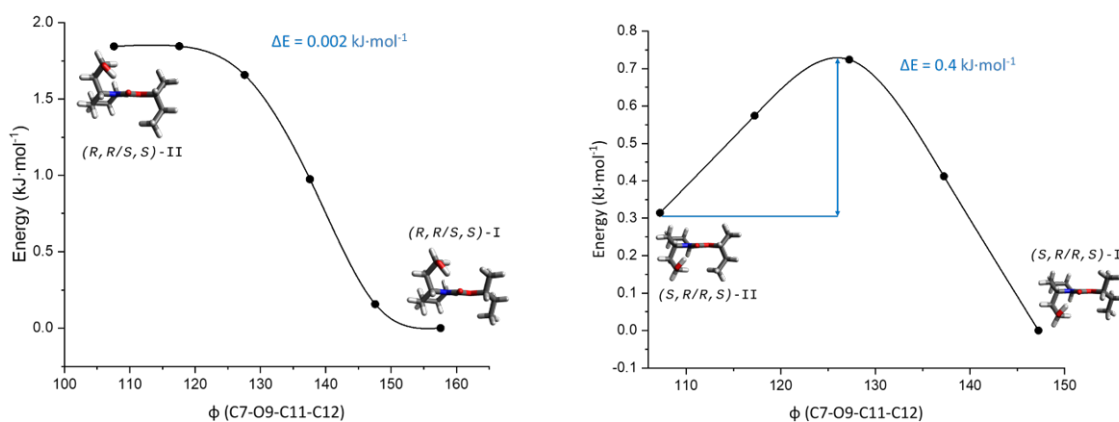


Figure S5. Potential energy scan for conformational relaxation from conformer III to I; V to I, VI to III; and IV to V for picaridin (R,R/S,S) at the B3LYP-D3(BJ)/def2-TZVP level of theory. The graph scans the δ (C10-C11-C12-C13) dihedral angle in steps of 10 degrees.

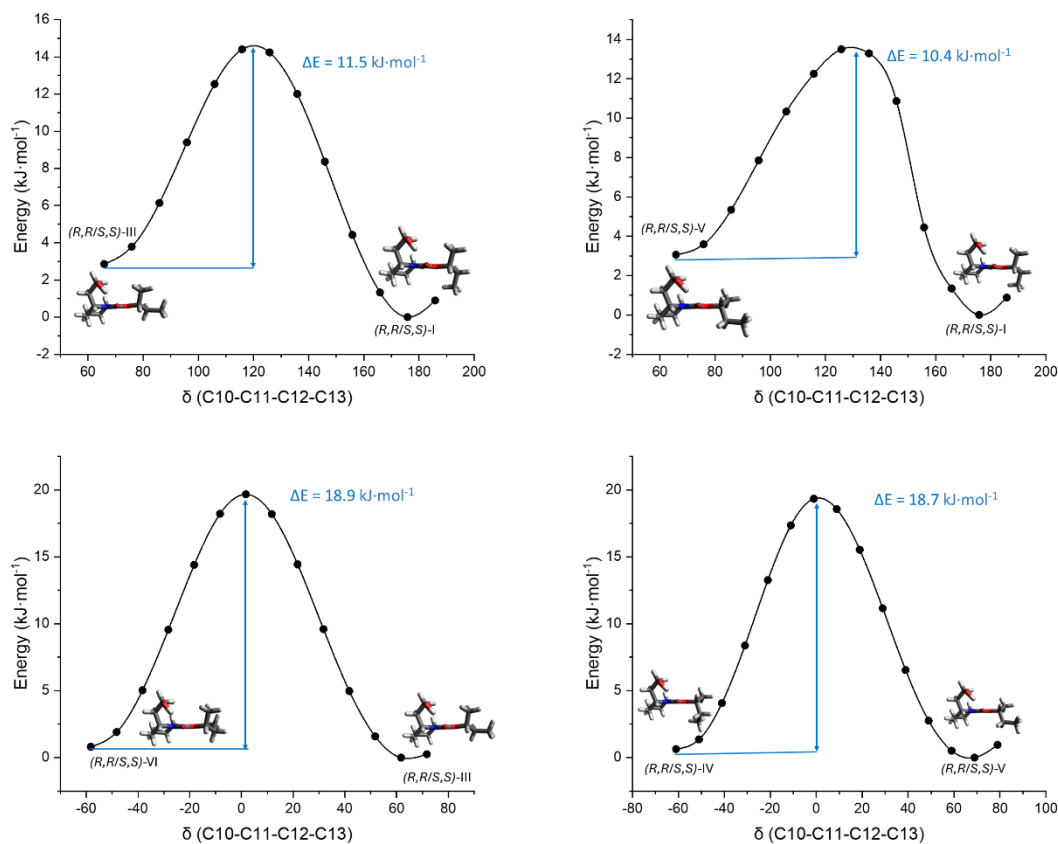


Figure S6. Potential energy scan for conformational relaxation from conformer III to II; IV to III, V to III; and VI to IV for picaridin (S,R/S,R) at the B3LYP-D3(BJ)/def2-TZVP level of theory. The graph scans the δ (C10-C11-C12-C13) or the ϕ (C7-O9-C11-C12) dihedral angles in steps of 10 degrees.

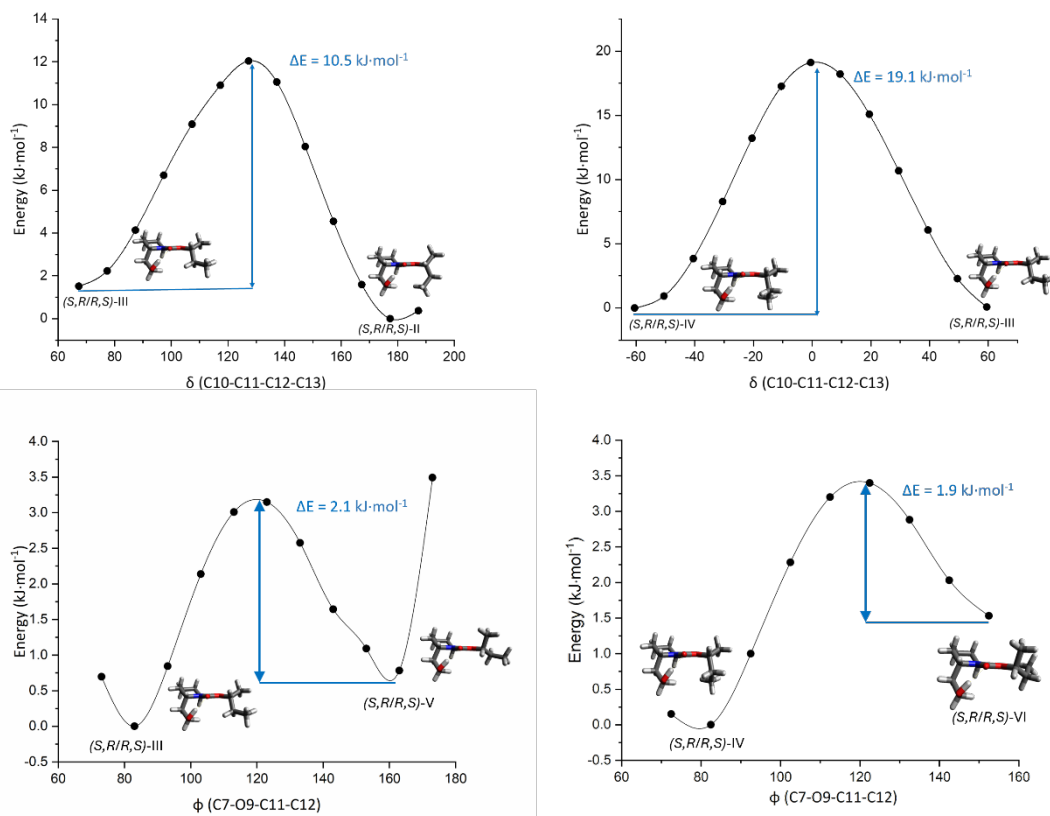


Table S1. Theoretical rotational parameters, dipole moments and planar moments of inertia for the picaridin (*R,R/S,S*) conformers at B3LYP-D3(BJ)/def2-TZVP. Relative energies to the most stable conformer considering the zero-point energy correction are given.

	I	II	III	IV	V	VI
<i>A</i> [MHz] ^a	710	699	790	716	757	732
<i>B</i> [MHz]	367	360	322	354	319	358
<i>C</i> [MHz]	273	292	253	280	264	272
<i>D_J</i> [kHz]	0.005	0.013	0.003	0.011	0.005	0.006
<i>D_{JK}</i> [kHz]	0.045	0.023	0.096	0.025	0.061	0.112
<i>D_K</i> [kHz]	0.077	0.109	0.144	0.082	0.121	0.018
χ_{aa} [MHz]	2.457	2.352	2.571	2.189	2.4862	2.5143
χ_{bb} [MHz]	-1.115	-1.343	-0.763	-0.798	-0.3847	-0.1295
χ_{cc} [MHz]	-1.341	-1.009	-1.809	-1.391	-2.1015	-2.3848
<i>P_{aa}</i> [uÅ ²]	1258	1206	1464	1263	1415	1290
<i>P_{bb}</i> [uÅ ²]	593	525	534	542	499	568
<i>P_{cc}</i> [uÅ ²]	119	198	106	164	169	122
$ \mu_a / \mu_b / \mu_c $ [D]	0.6/3.6/1.9	0.5/3.6/1.8	0.3/3.8/1.6	0.7/3.7/1.6	0.1/3.9/1.2	0.6/3.9/1.3
ΔE_{ZPE} [kJ/mol]	0.0	2.1	3.4	3.9	4.0	4.3

^a *A*, *B*, and *C* are the rotational constants; *D_J*, *D_{JK}*, and *D_K* are centrifugal distortion constants; χ_{aa} , χ_{bb} , and χ_{cc} are the quadrupole coupling constants for ¹⁴N; *P_{aa}*, *P_{bb}*, and *P_{cc}* are the planar moments of inertia calculated from the moments of inertia (*I_a*, *I_b*, and *I_c*) as for example *P_{cc}* = (*I_a*+*I_b*-*I_c*)/2), $|\mu_a|$, $|\mu_b|$, and $|\mu_c|$ are the absolute values for the dipole-moment component.

Table S2. Theoretical rotational parameters, dipole moments and planar moments of inertia for the picaridin (*S,R/R,S*) conformers at B3LYP-D3(BJ)/def2-TZVP. Relative energies to the most stable conformer considering the zero-point energy correction are given.

	I	II	III	IV	V	VI
<i>A</i> [MHz] ^a	708	721	781	735	776	727
<i>B</i> [MHz]	348	379	340	369	313	343
<i>C</i> [MHz]	292	292	263	293	258	274
<i>D_J</i> [kHz]	0.012	0.010	0.009	0.018	0.005	0.006
<i>D_{JK}</i> [kHz]	0.093	-0.001	-0.017	-0.005	0.006	0.009
<i>D_K</i> [kHz]	0.035	0.094	0.093	0.163	0.076	0.065
χ_{aa} [MHz]	2.373	2.315	2.262	2.180	2.400	2.278
χ_{bb} [MHz]	-0.726	-1.473	-0.703	-0.829	-0.540	0.189
χ_{cc} [MHz]	-1.647	-0.842	-1.559	-1.351	-1.860	-2.467
$ \mu_a / \mu_b / \mu_c $ [D]	0.3/4.0/1.5	0.1/3.7/2.0	0.5/3.7/1.7	0.1/3.7/1.8	0.3/4.0/1.5	0.9/4.1/1.1
<i>P_{aa}</i> [uÅ ²]	1235	1182	1380	1203	1461	1311
<i>P_{bb}</i> [uÅ ²]	496	549	541	521	498	533
<i>P_{cc}</i> [uÅ ²]	218	152	106	166	154	162
ΔE_{ZPE} [kJ/mol]	0.0	0.5	2.3	3.0	3.4	4.5

^a *A*, *B*, and *C* are the rotational constants; *D_J*, *D_{JK}*, and *D_K* are centrifugal distortion constants; χ_{aa} , χ_{bb} , and χ_{cc} are the quadrupole coupling constants for ¹⁴N; *P_{aa}*, *P_{bb}*, and *P_{cc}* are the planar moments of inertia calculated from the moments of inertia (*I_a*, *I_b*, and *I_c*) as for example *P_{cc}* = (*I_a*+*I_b*-*I_c*)/2), $|\mu_a|$, $|\mu_b|$, and $|\mu_c|$ are the absolute values for the dipole-moment component.

Table S3. Observed frequencies and residuals (MHz) for picaridin (*R,R/S,S*)-I for $J' K'_a K'_c F' \leftarrow J'' K''_a K''_c F''$ transitions.

J'	K'_a	K'_c	F'	J''	K''_a	K''_c	F''	Obs	Res	J'	K'_a	K'_c	F'	J''	K''_a	K''_c	F''	Obs	Res	J'	K'_a	K'_c	F'	J''	K''_a	K''_c	F''	Obs	Res
4	0	4	3	3	1	3	2	2242.1866	-0.0044	6	1	5	7	5	2	4	6	3392.1891	0.0083	3	3	0	2	2	2	1	1	3884.1640	0.0100
4	0	4	5	3	1	3	4	2242.1866	-0.0044	6	1	5	6	5	2	4	5	3392.3818	0.0073	3	3	0	4	2	2	1	3	3884.1640	0.0100
4	0	4	4	3	1	3	3	2242.3300	0.0055	7	2	5	6	6	3	4	5	3406.8221	0.0404	5	2	4	5	4	1	3	4	3901.4420	0.0011
2	2	1	2	1	1	0	1	2403.8088	-0.0084	7	2	5	8	6	3	4	7	3406.8221	0.0404	5	2	4	6	4	1	3	5	3901.5798	-0.0025
2	2	1	3	1	1	0	2	2404.1336	-0.0068	7	2	5	7	6	3	4	6	3407.0990	-0.0022	5	2	4	4	4	1	3	3	3901.5798	-0.0025
2	2	0	2	1	1	1	1	2516.0327	0.0048	6	0	6	7	5	1	5	6	3442.5671	-0.0258	7	0	7	8	6	1	6	7	4009.7544	0.0030
2	2	0	3	1	1	1	2	2516.4502	0.0057	6	0	6	5	5	1	5	4	3442.5671	-0.0258	7	0	7	6	6	1	6	5	4009.7544	0.0030
2	2	0	1	1	1	1	0	2516.4502	0.0057	6	0	6	6	5	1	5	5	3442.5671	-0.0258	7	0	7	7	6	1	6	6	4009.7544	0.0030
2	2	0	1	1	1	1	1	2517.1336	0.0184	4	2	3	4	3	1	2	3	3447.3881	0.0042	4	2	3	4	3	1	3	3	4015.7974	0.0022
4	1	4	3	3	0	3	2	2523.2016	0.0196	4	2	3	3	3	1	2	2	3447.5792	-0.0307	4	2	3	5	3	1	3	4	4016.1039	0.0048
4	1	4	5	3	0	3	4	2523.2016	0.0196	4	2	3	5	3	1	2	4	3447.5792	-0.0307	4	2	3	3	3	1	3	2	4016.2388	0.0058
3	1	2	3	2	0	2	2	2604.1114	0.0034	4	1	3	4	3	0	3	3	3460.2077	0.0085	7	1	7	6	6	0	6	5	4049.1423	0.0086
3	1	2	4	2	0	2	3	2604.3200	0.0014	4	1	3	5	3	0	3	4	3460.3599	0.0088	7	1	7	7	6	0	6	6	4049.1423	0.0086
3	1	2	2	2	0	2	1	2604.5597	0.0237	4	1	3	3	3	0	3	2	3460.4557	-0.0013	7	1	7	8	6	0	6	7	4049.1423	0.0086
5	1	4	6	4	2	3	5	2615.2035	0.0171	6	1	6	5	5	0	5	4	3524.2845	0.0023	7	1	6	8	6	2	5	7	4126.1370	-0.0010
5	1	4	4	4	2	3	3	2615.2035	0.0171	6	1	6	6	5	0	5	5	3524.2845	0.0023	7	1	6	6	6	2	5	5	4126.1370	-0.0010
5	1	4	5	4	2	3	4	2615.5286	0.0057	6	1	6	7	5	0	5	6	3524.2845	0.0023	7	1	6	7	6	2	5	6	4126.2653	0.0137
5	0	5	6	4	1	4	5	2856.6616	0.0012	4	2	2	4	3	1	2	3	3676.0650	0.0016	4	2	2	4	3	1	3	3	4244.4782	0.0034
5	0	5	4	4	1	4	3	2856.6616	0.0012	4	2	2	5	3	1	2	4	3676.2509	-0.0018	4	2	2	5	3	1	3	4	4244.7804	0.0037
5	0	5	5	4	1	4	4	2856.6616	0.0012	4	2	2	3	3	1	2	2	3676.3555	0.0088	4	2	2	3	3	1	3	2	4244.9344	0.0245
3	2	2	3	2	1	1	2	2950.1142	-0.0026	3	3	1	3	2	2	0	2	3864.7694	0.0002	8	2	6	7	7	3	5	6	4305.3503	-0.0077
3	2	2	4	2	1	1	3	2950.4147	0.0013	3	3	1	4	2	2	0	3	3864.9636	0.0074	8	2	6	9	7	3	5	8	4305.3503	-0.0077
3	2	2	2	2	1	1	1	2950.5790	0.0011	3	3	1	2	2	2	0	1	3864.9636	0.0074	8	2	6	8	7	3	5	7	4305.5634	-0.0105
3	2	1	3	2	1	1	2	3032.7501	-0.0017	3	3	0	3	2	2	0	2	3866.7567	0.0005	6	2	5	5	5	1	4	4	4325.9996	-0.0238
3	2	1	4	2	1	1	3	3033.0488	0.0043	3	3	0	2	2	2	0	1	3866.9558	0.0135	6	2	5	6	5	1	4	5	4325.9996	-0.0238
3	2	1	2	2	1	1	1	3033.2058	-0.0017	3	3	0	4	2	2	0	3	3866.9558	0.0135	6	2	5	7	5	1	4	6	4325.9996	-0.0238
3	2	1	3	2	1	2	2	3317.9129	0.0038	3	3	1	3	2	2	1	2	3881.9865	0.0029	5	2	3	5	4	1	3	4	4375.0064	-0.0038
3	2	1	4	2	1	2	3	3318.3136	0.0040	3	3	1	4	2	2	1	3	3882.1822	0.0144	5	2	3	4	4	1	3	3	4375.1448	-0.0121
3	2	1	2	2	1	2	1	3318.5413	0.0088	3	3	1	2	2	2	1	1	3882.1822	0.0144	5	2	3	6	4	1	3	5	4375.1448	-0.0121
6	1	5	5	5	2	4	4	3392.1891	0.0083	3	3	0	3	2	2	1	2	3883.9710	0.0005	5	1	4	5	4	0	4	4	4388.9914	-0.0022

J'	K _a '	K _c '	F'	J''	K _a ''	K _c ''	F''	Obs	Res
5	1	4	6	4	0	4	5	4389.1474	0.0004
5	1	4	4	4	0	4	3	4389.1474	0.0004
4	3	2	4	3	2	1	3	4469.9451	0.0007
4	3	2	3	3	2	1	2	4470.2295	-0.0033
4	3	2	5	3	2	1	4	4470.2295	-0.0033
4	3	1	4	3	2	1	3	4483.5913	0.0068
4	3	1	5	3	2	1	4	4483.8653	-0.0045
4	3	1	3	3	2	1	2	4483.8653	-0.0045
4	3	2	4	3	2	2	3	4552.5804	0.0010
4	3	2	3	3	2	2	2	4552.8598	-0.0034
4	3	2	5	3	2	2	4	4552.8598	-0.0034
8	0	8	9	7	1	7	8	4566.2752	0.0017
4	3	1	4	3	2	2	4	4566.2752	0.0017
8	0	8	8	7	1	7	7	4566.2752	0.0017
8	0	8	7	7	1	7	6	4566.2752	0.0017
4	3	1	5	3	2	2	4	4566.4985	-0.0019
4	3	1	3	3	2	2	2	4566.4985	-0.0019
8	1	8	9	7	0	7	8	4584.4221	0.0082
8	1	8	8	7	0	7	7	4584.4221	0.0082
8	1	8	7	7	0	7	6	4584.4221	0.0082
7	2	6	7	6	1	5	6	4742.9959	-0.0217
7	2	6	6	6	1	5	5	4743.0932	0.0300
7	2	6	8	6	1	5	7	4743.0932	0.0300
8	1	7	8	7	2	6	7	4805.5784	-0.0022
8	1	7	9	7	2	6	8	4805.5784	-0.0022
8	1	7	7	7	2	6	6	4805.5784	-0.0022
5	2	4	5	4	1	4	4	4838.5235	0.0029
5	2	4	4	4	1	4	3	4838.7793	-0.0119
5	2	4	6	4	1	4	5	4838.7793	-0.0119
5	3	3	5	4	2	2	4	5020.1630	0.0053

J'	K _a '	K _c '	F'	J''	K _a ''	K _c ''	F''	Obs	Res
5	3	3	6	4	2	2	5	5020.4046	-0.0007
5	3	3	4	4	2	2	3	5020.4046	-0.0007
5	3	2	5	4	2	2	4	5072.6019	0.0000
5	3	2	4	4	2	2	3	5072.8368	-0.0054
5	3	2	6	4	2	2	5	5072.8368	-0.0054
9	0	9	9	8	1	8	8	5117.3220	0.0062
9	0	9	10	8	1	8	9	5117.3220	0.0062
9	0	9	8	8	1	8	7	5117.3220	0.0062
9	1	9	10	8	0	8	9	5125.4093	0.0144
9	1	9	8	8	0	8	7	5125.4093	0.0036
9	1	9	9	8	0	8	8	5125.4093	0.0036
9	2	7	10	8	3	6	9	5176.4485	-0.0159
9	2	7	8	8	3	6	7	5176.4485	-0.0159
8	2	7	9	7	1	6	8	5176.6506	0.0138
8	2	7	7	7	1	6	6	5176.6506	0.0138
9	2	7	9	8	3	6	8	5176.6506	0.0138
8	2	7	8	7	1	6	7	5176.6506	0.0138
5	3	3	5	4	2	3	4	5248.8421	0.0048
5	3	3	6	4	2	3	5	5249.0786	-0.0041
5	3	3	4	4	2	3	3	5249.0786	-0.0041
4	4	1	4	3	3	0	3	5294.2829	0.0137
4	4	1	5	3	3	0	4	5294.4081	0.0247
4	4	1	3	3	3	0	2	5294.4081	0.0247
4	4	0	4	3	3	1	3	5296.4643	0.0186
4	4	0	3	3	3	1	2	5296.5721	0.0130
4	4	0	5	3	3	1	4	5296.5721	0.0130
5	3	2	5	4	2	3	4	5301.2836	0.0021
5	3	2	4	4	2	3	3	5301.5117	-0.0079
5	3	2	6	4	2	3	5	5301.5117	-0.0079
5	2	3	5	4	1	4	4	5312.0894	-0.0004

J'	K _a '	K _c '	F'	J''	K _a ''	K _c ''	F''	Obs	Res
5	2	3	6	4	1	4	5	5312.3434	-0.0224
5	2	3	4	4	1	4	3	5312.3434	-0.0224
6	1	5	6	5	0	5	5	5374.1944	0.0015
6	1	5	5	5	0	5	4	5374.3184	-0.0148
6	1	5	7	5	0	5	6	5374.3184	-0.0148
9	1	8	9	8	2	7	8	5435.3505	-0.0165
9	1	8	10	8	2	7	9	5435.3505	-0.0165
9	1	8	8	8	2	7	7	5435.3505	-0.0165
6	3	4	6	5	2	3	5	5504.7915	0.0095
6	3	4	5	5	2	3	4	5504.9523	-0.0242
6	3	4	7	5	2	3	6	5504.9523	-0.0242
9	2	8	8	8	1	7	7	5641.0883	0.0144
9	2	8	9	8	1	7	8	5641.0883	0.0144
9	2	8	10	8	1	7	9	5641.0883	0.0144
6	3	3	6	5	2	3	5	5651.2982	0.0023
6	3	3	5	5	2	3	4	5651.4465	-0.0312
6	3	3	7	5	2	3	6	5651.4465	-0.0312
10	0	10	10	9	1	9	9	5665.7123	0.0005
10	0	10	11	9	1	9	10	5665.7123	0.0005
10	0	10	9	9	1	9	8	5665.7123	0.0005
10	1	10	11	9	0	9	10	5669.2345	0.0060
10	1	10	10	9	0	9	9	5669.2345	0.0060
10	1	10	9	9	0	9	8	5669.2345	0.0060
7	3	5	7	6	2	4	6	5928.4160	0.0134
7	3	5	8	6	2	4	7	5928.5280	-0.0217
7	3	5	6	6	2	4	5	5928.5280	-0.0217
5	4	2	5	4	3	1	4	5932.8058	0.0019
5	4	2	4	4	3	1	3	5933.0071	-0.0019
5	4	2	6	4	3	1	5	5933.0071	-0.0019
5	4	1	5	4	3	1	4	5934.4911	0.0028

J'	K _a '	K _c '	F'	J''	K _a ''	K _c ''	F''	Obs	Res
5	4	1	6	4	3	1	5	5934.6886	-0.0044
5	4	1	4	4	3	1	3	5934.6886	-0.0044
5	4	2	5	4	3	2	4	5946.4451	0.0011
5	4	2	4	4	3	2	3	5946.6428	-0.0032
5	4	2	6	4	3	2	5	5946.6428	-0.0032
5	4	1	5	4	3	2	4	5948.1303	0.0019
5	4	1	4	4	3	2	3	5948.3210	-0.0091
5	4	1	6	4	3	2	5	5948.3210	-0.0091
7	2	6	7	7	1	7	7	2570.6531	0.0002
7	2	6	8	7	1	7	8	2570.8288	-0.0236
7	2	6	6	7	1	7	6	2570.8288	-0.0236
8	3	6	8	8	2	7	8	2614.6121	-0.0073
8	3	6	7	8	2	7	7	2614.7885	-0.0057
8	3	6	9	8	2	7	9	2614.7885	-0.0057
6	4	3	6	6	3	4	6	2704.5874	-0.0063
6	4	3	7	6	3	4	7	2704.9922	-0.0064
6	4	3	5	6	3	4	5	2704.9922	-0.0064
5	1	5	5	4	0	4	4	3015.3237	-0.0226
5	1	5	6	4	0	4	5	3015.3237	-0.0226
5	1	5	4	4	0	4	3	3015.3237	-0.0226
10	3	8	10	10	2	9	10	3219.6712	-0.0086
3	2	2	3	2	1	2	2	3235.2629	-0.0110
3	2	2	4	2	1	2	3	3235.6823	0.0037
3	2	2	2	2	1	2	1	3235.9044	0.0015
7	5	2	7	7	4	3	7	3413.7144	0.0041
7	5	2	8	7	4	3	8	3414.0972	-0.0108
7	5	2	6	7	4	3	6	3414.0972	-0.0108
9	5	5	9	9	4	6	9	3418.3838	0.0021
9	5	5	10	9	4	6	10	3418.6017	-0.0215
9	5	5	8	9	4	6	8	3418.6017	-0.0215

J'	K _a '	K _c '	F'	J''	K _a ''	K _c ''	F''	Obs	Res
10	1	9	10	10	0	10	10	3689.1494	0.0161
10	1	9	11	10	0	10	11	3689.2816	0.0148
10	1	9	9	10	0	10	9	3689.2816	0.0148
11	1	10	11	11	0	11	11	4111.5001	0.0218
11	1	10	10	11	0	11	10	4111.6333	0.0229
11	1	10	12	11	0	11	12	4111.5665	-0.0327
10	6	4	10	10	5	5	10	4119.9439	-0.0180
10	6	4	11	10	5	5	11	4120.2277	0.0167
10	6	4	9	10	5	5	9	4120.2277	0.0167
10	6	5	10	10	5	6	10	4160.5211	0.0097
10	6	5	11	10	5	6	11	4160.7588	0.0023
10	6	5	9	10	5	6	9	4160.7588	0.0023
9	6	4	9	9	5	5	9	4189.1692	0.0083
9	6	3	9	9	5	4	9	4174.7319	0.0045
9	6	3	10	9	5	4	10	4175.0004	-0.0290
9	6	3	8	9	5	4	8	4175.0004	-0.0290
8	6	2	8	8	5	3	8	4209.0567	-0.0003
8	6	2	7	8	5	3	7	4209.4933	0.0348
8	6	2	9	8	5	3	9	4209.4933	0.0348
8	6	2	7	8	5	3	7	4209.4933	0.0348
7	6	2	7	7	5	2	7	4230.7159	-0.0032
7	6	2	7	7	5	2	7	4230.7159	-0.0032
7	6	1	7	7	5	2	7	4230.7159	-0.0032
7	6	2	8	7	5	2	8	4231.2053	0.0013
7	6	1	8	7	5	2	8	4231.2053	0.0013
7	6	2	6	7	5	2	6	4231.2053	0.0013
7	6	1	6	7	5	2	6	4231.2053	0.0013
7	6	2	7	7	5	3	7	4231.7455	-0.0144
7	6	1	7	7	5	3	7	4231.7455	-0.0144
7	6	2	8	7	5	3	8	4232.2064	-0.0080

J'	K _a '	K _c '	F'	J''	K _a ''	K _c ''	F''	Obs	Res
7	6	1	8	7	5	3	8	4232.2064	-0.0080
7	3	5	6	6	3	4	5	4540.4417	0.0135
7	3	5	8	6	3	4	7	4540.4417	0.0135
7	3	5	7	6	3	4	6	4540.5558	-0.0006
11	7	5	11	11	6	6	11	4938.8884	0.0155
11	7	5	12	11	6	6	12	4939.1103	-0.0050
11	7	5	10	11	6	6	10	4939.1103	-0.0050
10	7	4	10	10	6	5	10	4968.0576	0.0000
10	7	4	11	10	6	5	11	4968.3381	-0.0102
10	7	4	9	10	6	5	9	4968.3381	-0.0102
6	2	5	6	5	1	5	5	5699.6354	0.0077
6	2	5	7	5	1	5	6	5699.8422	-0.0037
6	2	5	5	5	1	5	4	5699.8422	-0.0037
6	3	4	6	5	2	4	5	5978.3557	0.0043
6	3	4	7	5	2	4	6	5978.5239	-0.0272
6	3	4	5	5	2	4	4	5978.5239	-0.0272
10	2	8	9	9	3	7	8	5992.5961	-0.0412
10	2	8	11	9	3	7	10	5992.5961	-0.0412
10	2	8	10	9	3	7	9	5992.5961	-0.0412
7	2	5	7	6	1	5	6	5993.1131	-0.0149
7	2	5	8	6	1	5	7	5993.1131	-0.0149
7	2	5	6	6	1	5	5	5993.1131	-0.0149

Table S4. Observed frequencies and residuals (MHz) for picaridin (*S,R/R,S*)-I for $J' K'_a K'_c F' \leftarrow J'' K''_a K''_c F''$ transitions.

J'	K'_a	K'_c	F'	J''	K''_a	K''_c	F''	Obs	Res	J'	K'_a	K'_c	F'	J''	K''_a	K''_c	F''	Obs	Res	J'	K'_a	K'_c	F'	J''	K''_a	K''_c	F''	Obs	Res
3	1	3	3	2	0	2	2	2142.1144	0.0064	7	2	5	6	6	3	4	5	2965.2965	0.0146	11	5	7	11	11	4	8	11	3422.2778	0.0133
3	1	3	4	2	0	2	3	2142.1144	0.0064	7	2	5	8	6	3	4	7	2965.2965	0.0146	11	5	7	12	11	4	8	12	3422.4414	0.0112
3	1	3	2	2	0	2	1	2142.2544	0.0114	7	2	5	7	6	3	4	6	2965.4901	-0.0025	11	5	7	10	11	4	8	10	3422.4414	0.0112
6	2	4	7	5	3	3	6	2174.6285	-0.0021	3	2	2	3	2	1	1	2	2998.7078	0.0022	4	2	3	3	3	1	2	2	3554.1665	-0.0257
6	2	4	5	5	3	3	4	2174.6285	-0.0021	3	2	2	2	2	1	1	1	2998.8820	-0.0224	4	2	3	4	3	1	2	3	3554.1665	-0.0257
6	2	4	6	5	3	3	5	2174.9998	-0.0109	3	2	2	4	2	1	1	3	2998.8820	-0.0224	4	2	3	5	3	1	2	4	3554.1665	-0.0257
4	0	4	5	3	1	3	4	2257.0598	-0.0220	3	2	1	3	2	1	1	2	3028.3166	0.0060	6	0	6	6	5	1	5	5	3556.9417	0.0282
4	0	4	3	3	1	3	2	2257.0598	-0.0220	3	2	1	4	2	1	1	3	3028.5350	-0.0002	6	1	6	7	5	0	5	6	3755.1185	-0.0010
4	0	4	4	3	1	3	3	2257.1808	0.0214	3	2	1	2	2	1	1	1	3028.6660	0.0177	6	1	6	6	5	0	5	5	3755.1185	-0.0010
6	4	2	6	6	3	3	6	2665.6516	-0.0107	13	3	11	13	13	2	12	13	3164.6771	-0.0071	6	1	6	5	5	0	5	4	3755.1185	-0.0010
6	4	2	5	6	3	3	5	2666.0479	-0.0042	13	3	11	12	13	2	12	12	3164.8805	-0.0078	8	2	6	7	7	3	5	6	3782.4412	-0.0164
6	4	2	7	6	3	3	7	2666.0479	-0.0042	13	3	11	14	13	2	12	14	3164.8805	-0.0078	8	2	6	9	7	3	5	8	3782.4412	-0.0164
4	1	4	5	3	0	3	4	2682.9768	0.0097	3	2	2	3	2	1	2	2	3166.0653	-0.0011	8	2	6	8	7	3	5	7	3782.5669	-0.0012
4	1	4	3	3	0	3	2	2682.9768	0.0097	3	2	2	4	2	1	2	3	3166.6247	0.0032	3	3	1	3	2	2	0	2	3855.4240	-0.0018
4	1	4	4	3	0	3	3	2682.9768	0.0097	3	2	2	2	2	1	2	1	3166.9241	-0.0056	3	3	1	4	2	2	0	3	3855.6193	0.0362
5	4	1	5	5	3	2	5	2689.0542	-0.0213	6	1	5	5	5	2	4	4	3173.4231	-0.0092	3	3	1	2	2	2	0	1	3855.6193	0.0362
5	4	1	6	5	3	2	6	2689.5891	-0.0115	6	1	5	7	5	2	4	6	3173.4231	-0.0092	3	3	0	3	2	2	1	2	3861.8355	0.0001
5	4	1	4	5	3	2	4	2689.7101	0.0025	6	1	5	6	5	2	4	5	3173.5478	0.0104	3	3	0	2	2	2	1	1	3862.0466	0.0247
6	4	3	6	6	3	4	6	2697.4480	-0.0061	3	2	1	3	2	1	2	2	3195.6784	0.0070	3	3	0	4	2	2	1	3	3862.0466	0.0247
6	4	3	5	6	3	4	5	2697.8541	-0.0155	3	2	1	4	2	1	2	3	3196.2866	0.0044	4	2	2	4	3	1	3	3	3974.7179	-0.0012
6	4	3	7	6	3	4	7	2697.8541	-0.0155	3	2	1	2	2	1	2	1	3196.6209	0.0109	4	2	2	5	3	1	3	4	3975.2789	0.0055
7	4	4	7	7	3	5	7	2698.2901	-0.0035	5	1	5	4	4	0	4	3	3217.1320	0.0048	4	2	2	3	3	1	3	2	3975.4900	0.0025
7	4	4	6	7	3	5	6	2698.5869	-0.0214	5	1	5	6	4	0	4	5	3217.1320	0.0048	5	1	4	5	4	0	4	4	4043.9802	0.0025
7	4	4	8	7	3	5	8	2698.5869	-0.0214	5	1	5	5	4	0	4	4	3217.1320	0.0048	5	1	4	6	4	0	4	5	4044.3073	-0.0016
9	4	6	9	9	3	7	9	2727.6529	0.0095	4	1	3	4	3	0	3	3	3238.7349	0.0011	5	1	4	4	4	0	4	3	4044.4393	0.0165
9	4	6	10	9	3	7	10	2727.8651	0.0111	4	1	3	5	3	0	3	4	3239.0777	0.0062	5	2	4	6	4	1	3	5	4082.2948	0.0112
9	4	6	8	9	3	7	8	2727.8651	0.0111	4	1	3	3	3	0	3	2	3239.2392	0.0060	5	2	4	4	4	1	3	3	4082.2948	0.0112
5	0	5	6	4	1	4	5	2915.9097	0.0304	9	5	4	9	9	4	5	9	3415.9459	-0.0065	5	2	4	5	4	1	3	4	4082.2948	0.0112
5	0	5	4	4	1	4	3	2915.9097	0.0304	9	5	4	8	9	4	5	8	3416.1779	-0.0043	7	0	7	7	6	1	6	6	4180.3200	0.0064
5	0	5	5	4	1	4	4	2915.9097	0.0304	9	5	4	10	9	4	5	10	3416.1779	-0.0043	7	0	7	8	6	1	6	7	4180.3200	0.0064

J'	K _a '	K _c '	F'	J''	K _a ''	K _c ''	F''	Obs	Res
7	0	7	6	6	1	6	5	4180.3200	0.0064
7	1	7	8	6	0	6	7	4303.1240	-0.0160
7	1	7	7	6	0	6	6	4303.1240	-0.0160
7	1	7	6	6	0	6	5	4303.1240	-0.0160
4	3	2	4	3	2	1	3	4482.5602	0.0030
4	3	2	5	3	2	1	4	4482.8030	-0.0106
4	3	2	3	3	2	1	2	4482.8030	-0.0106
4	3	1	4	3	2	1	3	4485.3933	0.0018
4	3	1	5	3	2	1	4	4485.6382	-0.0075
4	3	1	3	3	2	1	2	4485.6382	-0.0075
4	3	2	4	3	2	2	3	4512.1642	0.0021
4	3	2	5	3	2	2	4	4512.4659	-0.0083
4	3	2	3	3	2	2	2	4512.4659	-0.0083
4	3	1	4	3	2	2	3	4514.9982	0.0019
4	3	1	3	3	2	2	2	4515.3142	-0.0090
4	3	1	5	3	2	2	4	4515.3142	-0.0090
6	2	5	6	5	1	4	5	4586.3677	-0.0221
6	2	5	5	5	1	4	4	4586.3677	-0.0221
5	2	4	5	4	1	4	4	4638.0306	0.0085
5	2	4	6	4	1	4	5	4638.4245	0.0106
5	2	4	4	4	1	4	3	4638.5482	0.0078
8	1	7	8	7	2	6	7	4677.2995	-0.0110
8	1	7	7	7	2	6	6	4677.2995	-0.0110
8	1	7	9	7	2	6	8	4677.2995	-0.0110
8	0	8	7	7	1	7	6	4789.6079	0.0058
8	0	8	8	7	1	7	7	4789.6079	0.0058
8	0	8	9	7	1	7	8	4789.6079	0.0058
5	2	3	5	4	1	4	4	4827.5846	0.0047
5	2	3	6	4	1	4	5	4828.1205	0.0093
5	2	3	4	4	1	4	3	4828.2631	-0.0030

J'	K _a '	K _c '	F'	J''	K _a ''	K _c ''	F''	Obs	Res
8	1	8	7	7	0	7	6	4862.2375	-0.0166
8	1	8	9	7	0	7	8	4862.2375	-0.0166
8	1	8	8	7	0	7	7	4862.2375	-0.0166
6	2	4	6	5	1	4	5	4936.1477	0.0034
6	2	4	5	5	1	4	4	4936.2599	-0.0235
6	2	4	7	5	1	4	6	4936.2599	-0.0235
7	2	6	8	6	1	5	7	5072.3859	-0.0038
7	2	6	7	6	1	5	6	5072.3859	-0.0038
5	3	3	5	4	2	2	4	5087.5504	-0.0010
5	3	3	6	4	2	2	5	5087.7091	-0.0209
5	3	3	4	4	2	2	3	5087.7091	-0.0209
5	3	2	5	4	2	2	4	5098.7521	0.0072
5	3	2	6	4	2	2	5	5098.9252	-0.0113
5	3	2	4	4	2	2	3	5098.9252	-0.0113
5	3	3	5	4	2	3	4	5173.5134	-0.0017
5	3	3	6	4	2	3	5	5173.7920	-0.0086
5	3	3	4	4	2	3	3	5173.7920	-0.0086
5	3	2	5	4	2	3	4	5184.7110	0.0024
5	3	2	6	4	2	3	5	5185.0076	-0.0067
5	3	2	4	4	2	3	3	5185.0076	-0.0067
4	4	1	4	3	3	0	3	5273.8427	0.0021
4	4	1	5	3	3	0	4	5273.9678	0.0197
4	4	1	3	3	3	0	2	5273.9678	0.0197
4	4	0	4	3	3	1	3	5274.2828	0.0121
4	4	0	3	3	3	1	2	5274.4046	0.0251
4	4	0	5	3	3	1	4	5274.4046	0.0251
9	0	9	9	8	1	8	8	5388.9640	0.0033
9	0	9	10	8	1	8	9	5388.9640	0.0033
9	0	9	8	8	1	8	7	5388.9640	0.0033
9	1	8	8	8	2	7	7	5397.9733	-0.0131

J'	K _a '	K _c '	F'	J''	K _a ''	K _c ''	F''	Obs	Res
9	1	8	9	8	2	7	8	5397.9733	-0.0131
9	1	8	10	8	2	7	9	5397.9733	-0.0131
6	2	5	6	5	1	5	5	5413.2311	0.0100
6	2	5	5	5	1	5	4	5413.5813	-0.0264
6	2	5	7	5	1	5	6	5413.5813	-0.0264
8	2	7	9	7	1	6	8	5549.2352	-0.0145
8	2	7	8	7	1	6	7	5549.2352	-0.0145
6	3	4	6	5	2	3	5	5660.1582	0.0105
6	3	4	5	5	2	3	4	5660.2527	0.0050
6	3	4	7	5	2	3	6	5660.2527	0.0050
6	3	3	6	5	2	3	5	5692.9603	0.0026
6	3	3	7	5	2	3	6	5693.0829	-0.0017
6	3	3	5	5	2	3	4	5693.0829	-0.0017
6	2	4	6	5	1	5	5	5762.9464	-0.0081
6	2	4	7	5	1	5	6	5763.4747	-0.0064
6	2	4	5	5	1	5	4	5763.6134	0.0105
6	3	4	6	5	2	4	5	5849.7097	0.0043
6	3	3	6	5	2	4	5	5882.5227	0.0073
6	3	3	5	5	2	4	4	5882.7983	-0.0005
6	3	3	7	5	2	4	6	5882.7983	-0.0005
5	4	2	5	4	3	1	4	5913.6909	-0.0013
5	4	2	4	4	3	1	3	5913.8891	-0.0075
5	4	2	6	4	3	1	5	5913.8891	-0.0075
5	4	1	5	4	3	2	4	5916.7296	-0.0020
5	4	1	6	4	3	2	5	5916.9314	-0.0100
5	4	1	4	4	3	2	3	5916.9314	-0.0100