Electronic Supplementary Material (ESI) for Physical Chemistry Chemical Physics.

Absolute Configuration Assignment of Two Hybrid Isoindolinone-Phthalide Molecules by Vibrational Circular Dichroism

Supporting Information

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Table S1: Enthalpies in kcal mol^{-1} of conformers of 1 computed at the SCRF-ωB97XD/6-31G* level. Enthalpies with superscript (b) have been computed at the same level but with an ultrafine integration grid and tight convergence criteria in the geometry optimization procedure.
***Labeling of conformations d and e of Ref.[1] as T^-C^- and T^+C^- is only based on visual inspection of the schemes published. Conformers are labeled according to the values of the dihedral angles H-C6-C6′-C1′ and C3′-C4′-O-C7′ (Scheme 1), using letters T and C for angles closer to 180° and 0°, followed by a ± sign, indicating their sign.[2]**

	Ref.[1]		This work		
AC	Label	$H_{298}^{(a}$)	$H_{298}^{(a)}$	$H_{298}^{(b)}$	Label
	a	0	0	0	C^+C^-
	b	0.003	0.003	0.001	C^-C^-
	c	0.033	0.034	-0.001	C^+C^+
	d	0.274			T^-C^{-*}
(R,R)			-	0.358	T^-C^+
	e	0.366	-		T^+C^{-*}
			0.435	0.451	T^+C^-
	f	0.464	0.462	0.383	T^+C^+
			0.545	0.407	T^-C^-
	a	0	0	0	T^-C^-
(R,S)	b	0.043	0.042	0.028	T^-C^+
			0.305	0.266	C^+C^-
	c	0.346	0.348	0.203	C^+C^+

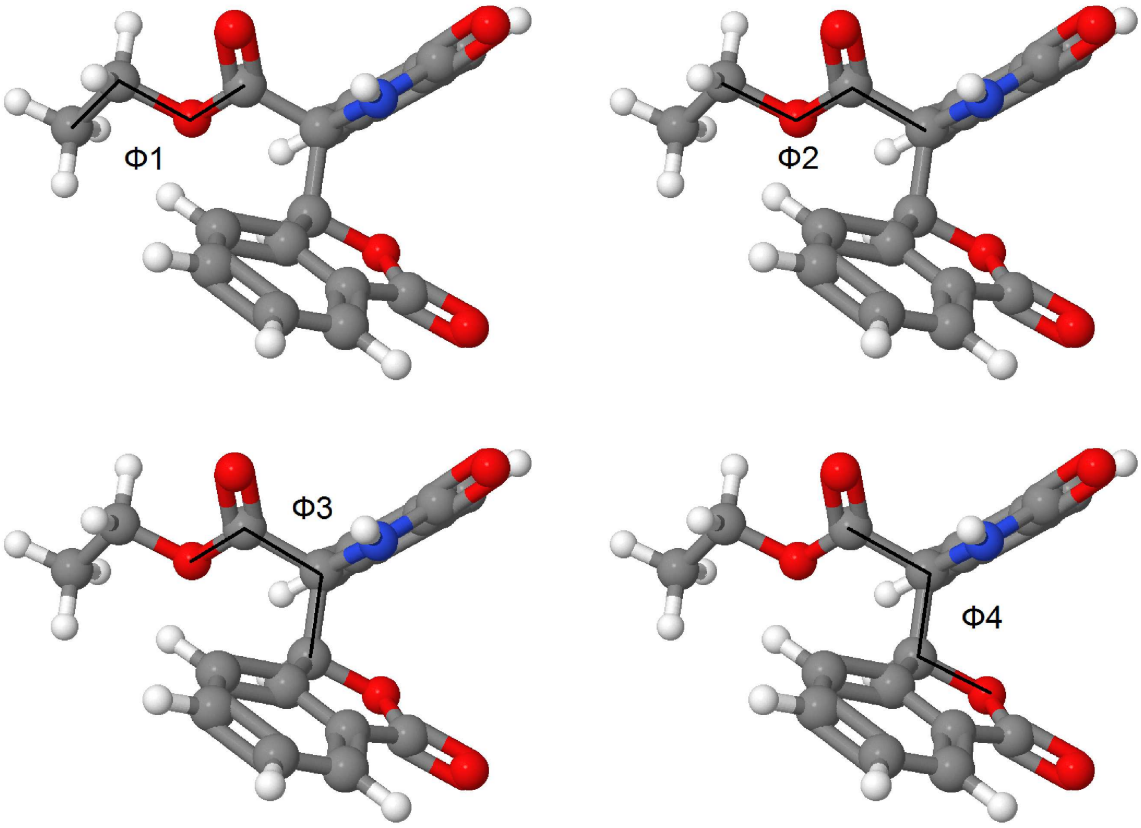

Figure S1: Relevant torsion angles for the conformers of **2** and **3**.

Table S2: Relative energies and relevant dihedral angles of the conformers studied for (*S*,*S*)-2 and (*S*,*S*)-3

	E (kcal mol^{-1})		ϕ_1		ϕ_2		ϕ_3		ϕ_4	
	2	**3**	**2**	**3**	**2**	**3**	**2**	**3**	**2**	**3**
1	0.00	0.00	-177.8	-178.5	175.8	176.1	-100.3	-100.9	59.9	60.3
2	0.09	0.09	-84.3	-84	174.2	174.7	-100.4	-100.3	59.4	60
3	0.26	0.22	86.6	86.5	176.8	176.8	-101.8	-101.6	60.5	60.8
4	0.38	0.38	-178.2	-179	175.8	175.9	146.9	148	172.5	173.3
5	0.53	0.56	-85.9	-84.9	175.5	175.4	145.4	148.6	172.6	173
6	0.81	0.81	89.6	89.6	175	175	149.5	151.4	172.1	172.6
7	1.17	1.16	177.7	178.9	-178.9	-179	67.5	67.8	55.6	55.8
8	1.21	1.19	84.6	85.6	-178	-178.4	66.8	68.7	54.9	56.1
9	1.28	1.26	-84.8	-85.9	-179.3	-179.4	68.2	67.7	55.7	56.2
10	1.44	1.56	178.8	179.3	-177.8	-177.7	-55.5	-55.6	175.4	175.8
11	1.49	1.61	83.9	84.1	-177.4	-177.5	-55.7	-56.6	175.4	175.3
12	1.80	1.46	179.7	178.5	-178.8	-178.5	117.6	116.9	-59.4	-58.1
13	1.83	1.44	94.2	95.2	-175.6	-175.5	118.6	117.3	-55.8	-54.5
14	1.86	1.99	-85.7	-85.9	-174.7	-174.5	-55.2	-55.4	173.4	173.9
15	2.10	1.71	-85.2	-85.9	-179.4	-179.2	119.2	117.7	-59.4	-58.7
16	2.99	2.68	179.7	-179.9	178.9	178.7	-59	-59.4	-50.8	-50.4
17	3.08	2.81	-81.3	-82	-179.1	-178.9	-55	-56.4	-49.1	-47.8
18	3.17	2.89	84.2	84.7	179.2	179.2	-59.3	-59.7	-51	-50.6

Table S3: Relative energies and relevant dihedral angles of the conformers studied for (*R*,*S*)-2 and (*R*,*S*)-3

	E (kcal mol^{-1})		ϕ_1		ϕ_2		ϕ_3		ϕ_4	
	2	**3**	**2**	**3**	**2**	**3**	**2**	**3**	**2**	**3**
1	0.00	0.00	178.6	180	-179.2	-179.1	124.7	124	-62.7	-63
2	0.14	0.15	86.2	86.2	-177.9	-177.7	124.2	123.1	-62	-62.1
3	0.23	0.24	-86.4	-86.1	179.7	-179.8	126.1	124.4	-63.4	-63.2
4	0.59	0.37	-173.6	-172.8	176.2	175.5	-68.1	-69.6	67.8	67.5
5	0.71	0.80	-178.2	-177.7	178.5	178.3	-55.5	-56.1	-55	-54.8
6	0.75	1.09	-84.8	-84.8	177.5	177.5	-56	-55.9	-54.6	-54.6
7	0.85	1.19	84.8	84.6	178.7	179	-55.9	-56.1	-55.5	-55.3
8	0.99	0.81	-87.3	-87.5	178.7	178.5	-74.4	-74.8	65.6	65.9
9	1.29	1.12	85.8	86.1	177.8	178	-68.8	-69.2	68.3	68.7
10	2.55	2.91	178.2	179.3	-177.7	-178.1	106.7	108.1	63.6	63.5
11	2.66	3.08	84.9	85.3	-178.4	-178.6	107.8	109.8	63.4	63.9
12	2.74	3.04	-84.6	-84.7	-179.4	-179.6	113.5	115.5	63.9	65
13	3.73	3.99	179.9	178	-174.2	-174.5	-162.2	-166.9	-172.2	-171.9
14	3.95	3.82	84.8	85.5	-173.6	-173.4	-161.9	-161.3	-172.1	-172
15	4.15	4.05	-88.4	-88.9	-174.1	-174	-165.3	-164.2	-171.7	-171.9
16	4.76	4.48	-177.7	-177.5	-179.3	-179.3	80.9	80.6	-173.6	-173.6
17	4.85	4.57	-84.8	-84.8	179.8	179.9	79	79.6	-174.4	-173.9
18	5.20	4.91	90.9	91.1	179.9	-179.9	83.9	83.2	-173	-172.4

Table S4: Some results of the non-linear least squares fits of the VA spectra by sums of Lorentzians: number of Lorentzians, estimates of the experimental error, GOFIs described in the text, and rounded mean value of half-width at half-maximum γ in cm^{-1}. The estimates of the experimental error are either in units of absorbance A or in units of molar extinction coefficient ϵ (M^{-1} cm^{-1}).

Species	L	σ^{A}_{exp}	σ^{ϵ}_{exp}	RMSE	MAE	$\cos\theta$	γ
(R,R)-**1**	37	0.0048	9.24	1	0.531	0.999	4
(S,R)-**1**	34	0.0053	10.28	1	0.543	0.999	4
(S^*,R^*)-**2**	32	0.0032	3.42	1	0.606	0.999	5
(ξ,ξ')-**3**	35	0.0015	1.96	1	0.486	1.000	6

Table S5: Some results of the non-linear least squares fits of the VCD spectra by sums of Lorentzians: number of Lorentzians, estimates of the experimental error, GOFIs described in the text, and rounded mean value of half-width at half-maximum γ in cm^{-1}. The estimates of the experimental error are either in units of differential absorbance ΔA or in units of differential molar extinction coefficient $\Delta\epsilon$ (M^{-1} cm^{-1}).

Species	L	$\sigma^{\Delta A}_{exp}$	$\sigma^{\Delta\epsilon}_{exp}$	RMSE	MAE	$\cos\theta$	SI	ESI	γ
(R,R)-**1**	32	8.87e-07	0.0017	1	0.582	0.994	0.994	0.994	4
(S,R)-**1**	35	9.61e-07	0.0019	1	0.455	0.995	0.996	0.996	4
(S^*,R^*)-**2**	48	6.38e-07	0.0007	1	0.523	0.992	0.993	0.993	4
(ξ,ξ')-**3**	44	4.78e-07	0.0006	1	0.564	0.998	0.998	0.998	4

Table S6: Frequency Scaling Factors λ obtained by best fit between experimental spectra and the EP-calculated spectra of two diastereomers.

Species	(R^*,R^*)	(S^*,R^*)
(R,R)-**1**	0.954	0.954
(S,R)-**1**	0.954	0.954
(S^*,R^*)-**2**	0.971	0.976
(ξ,ξ')-**3**	0.972	0.976

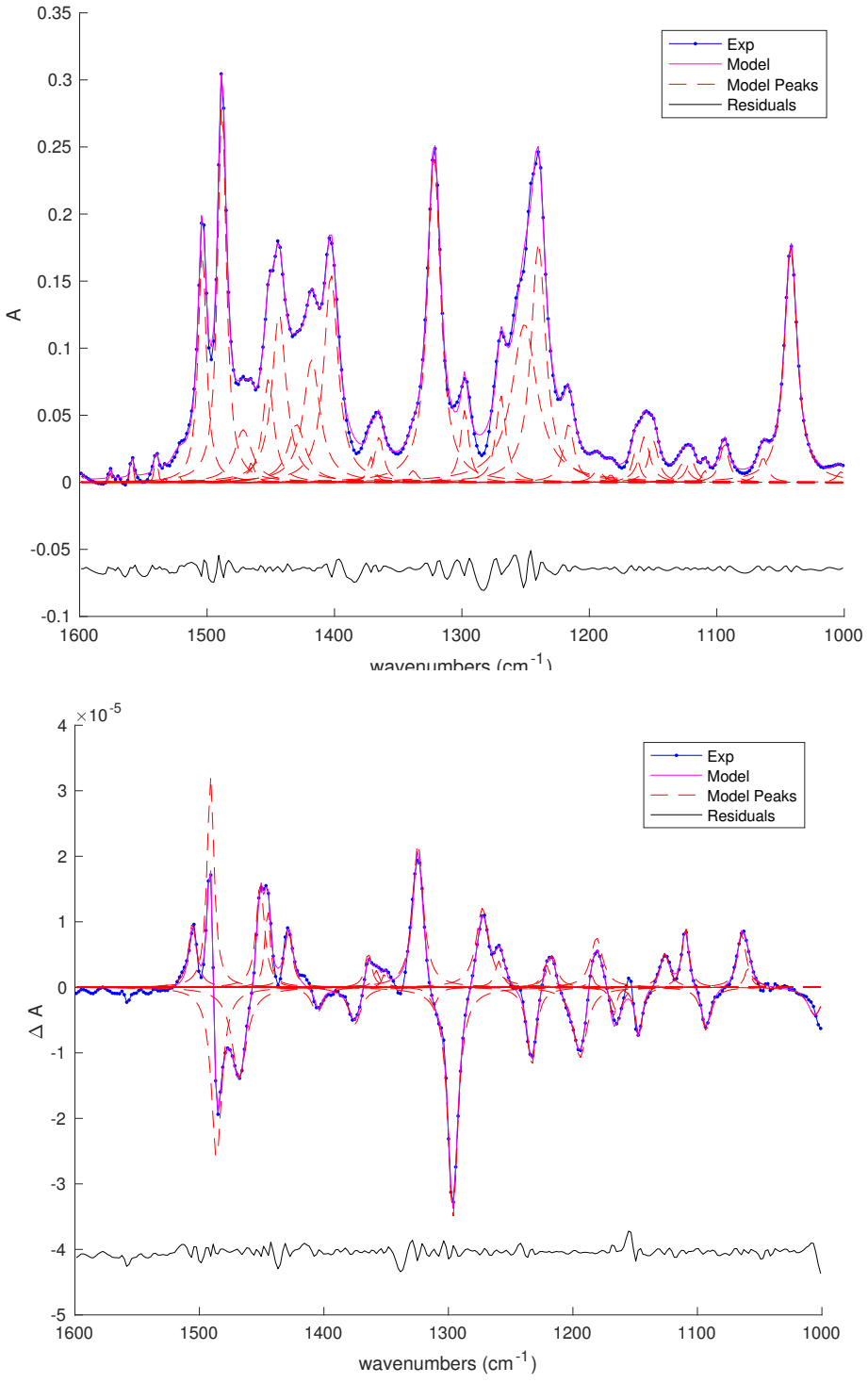

Figure S2: Experimental VA and VCD spectrum of (*R*,*R*)-**1** and their fit with Lorentzian peaks. Residuals are shifted downwards on the same scale.

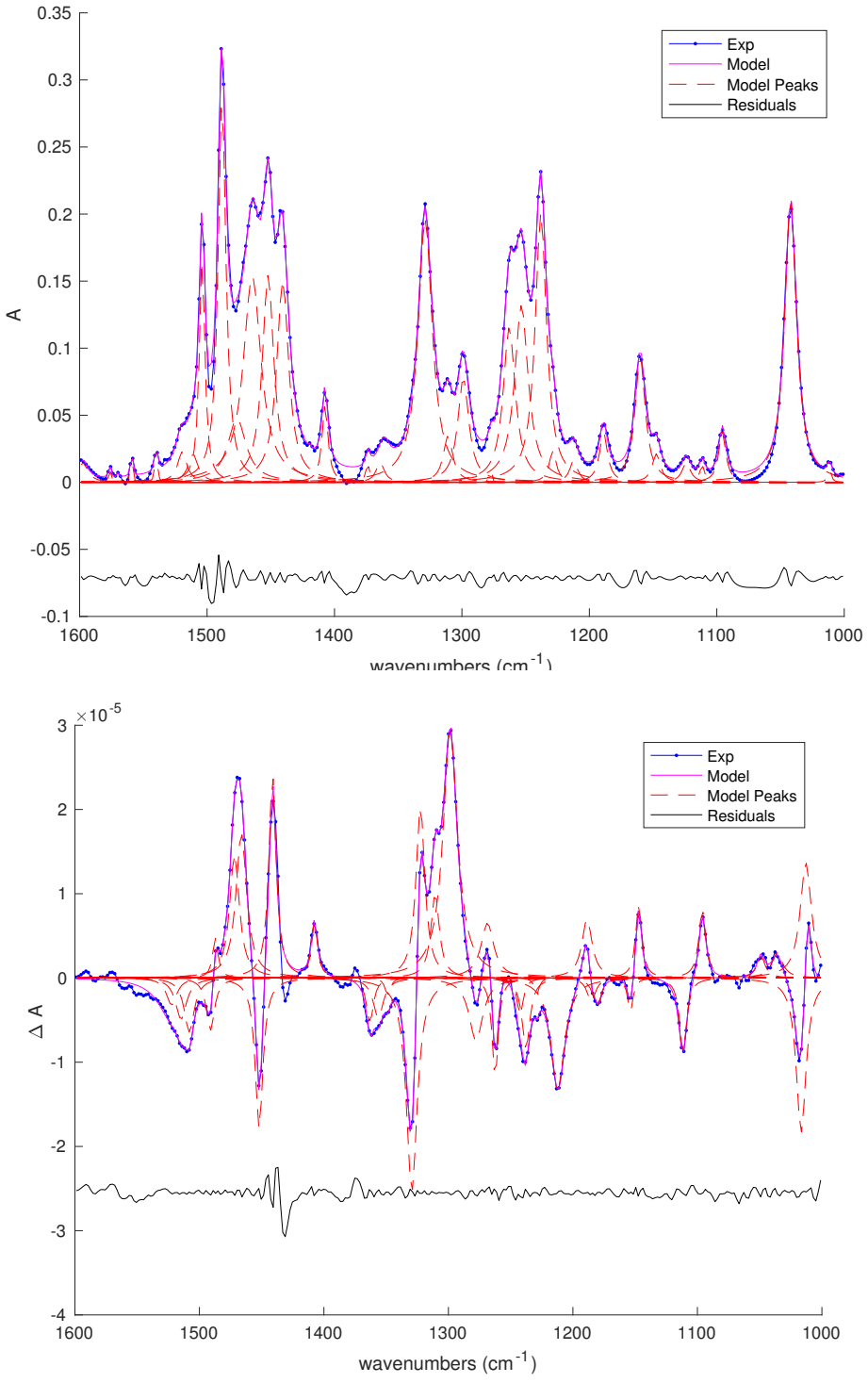

Figure S3: Experimental VA and VCD spectrum of (*S*,*R*)-**1** and their fit with Lorentzian peaks. Residuals are shifted downwards on the same scale.

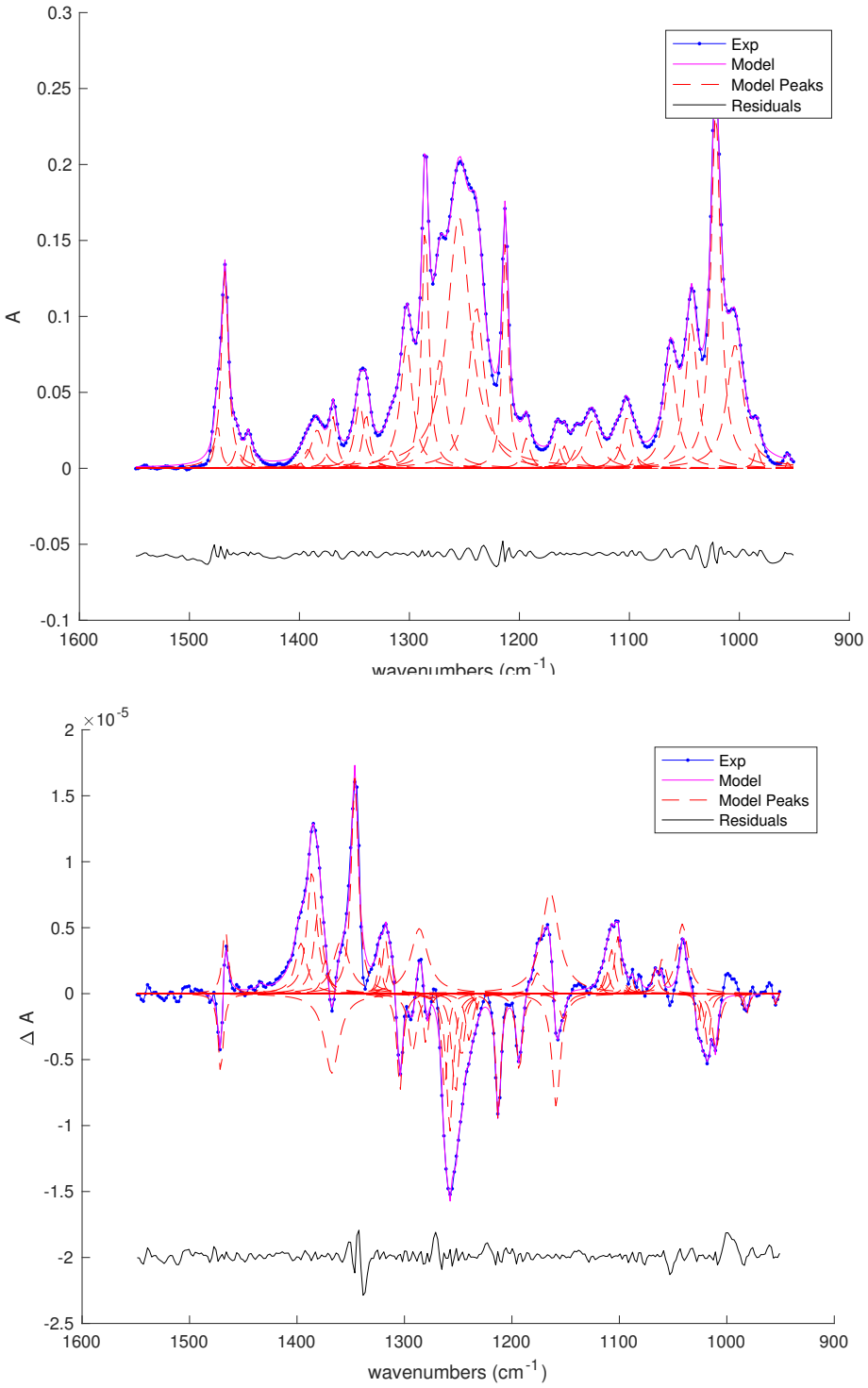

Figure S4: Experimental VA and VCD spectrum of (R^*,S^*)-**2** and their fit with Lorentzian peaks. Residuals are shifted downwards on the same scale.

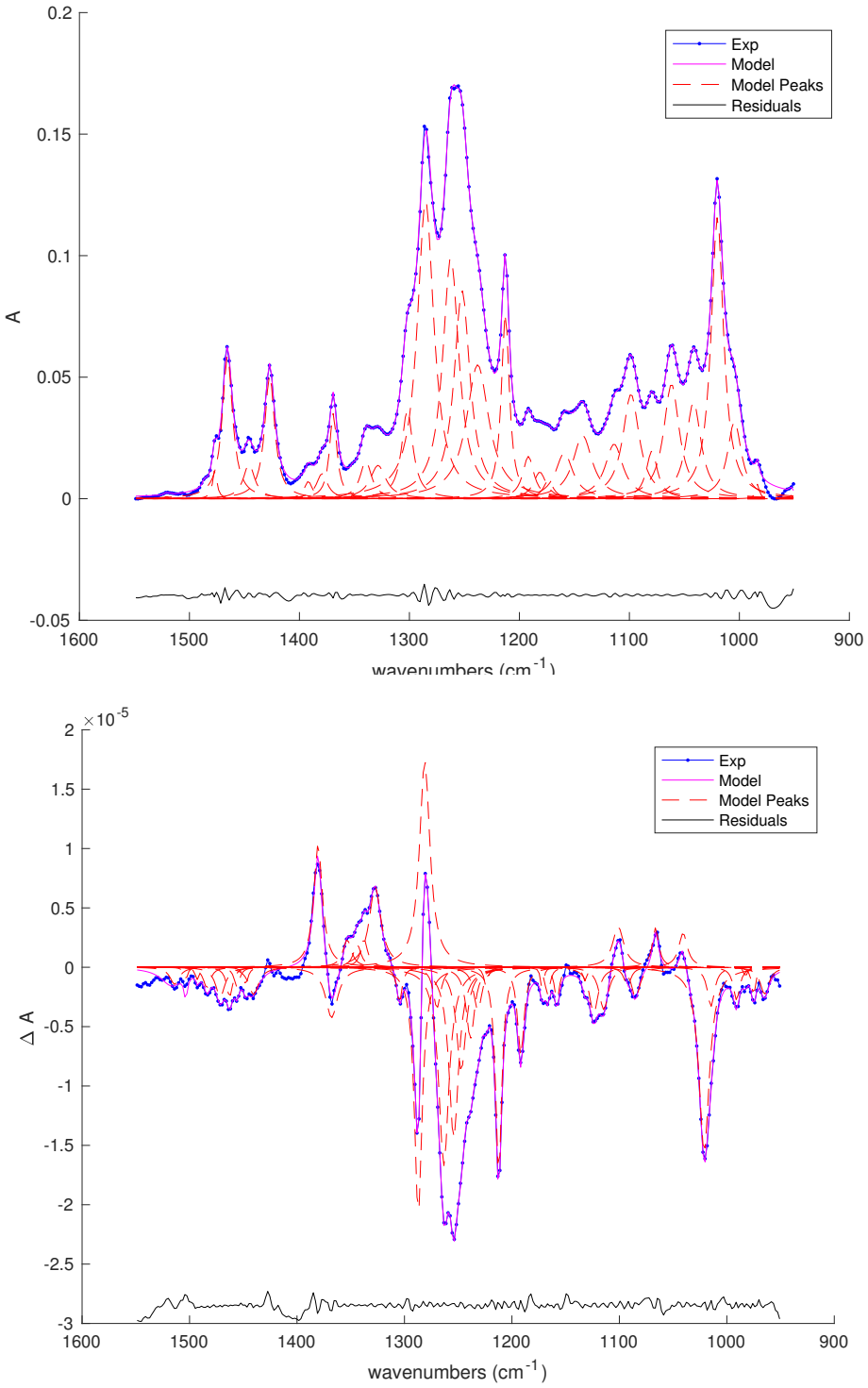

Figure S5: Experimental VA and VCD spectrum of (ξ,ξ')-**3** and their fit with Lorentzian peaks. Residuals are shifted downwards on the same scale.

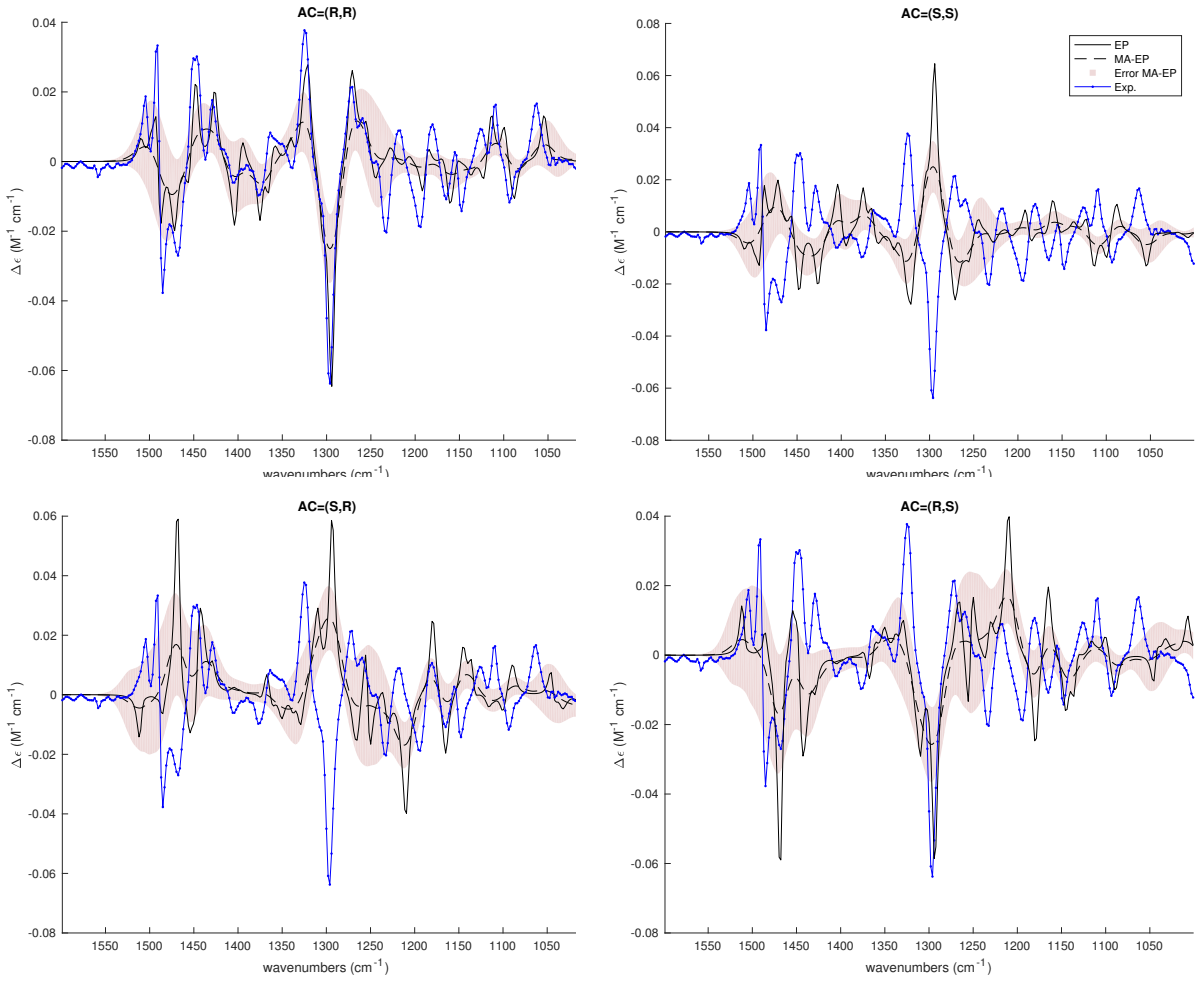

Figure S6: VCD spectrum of (*R*,*R*)-**1** and its fit with EP and MA-EP methods for all 4 possible ACs.

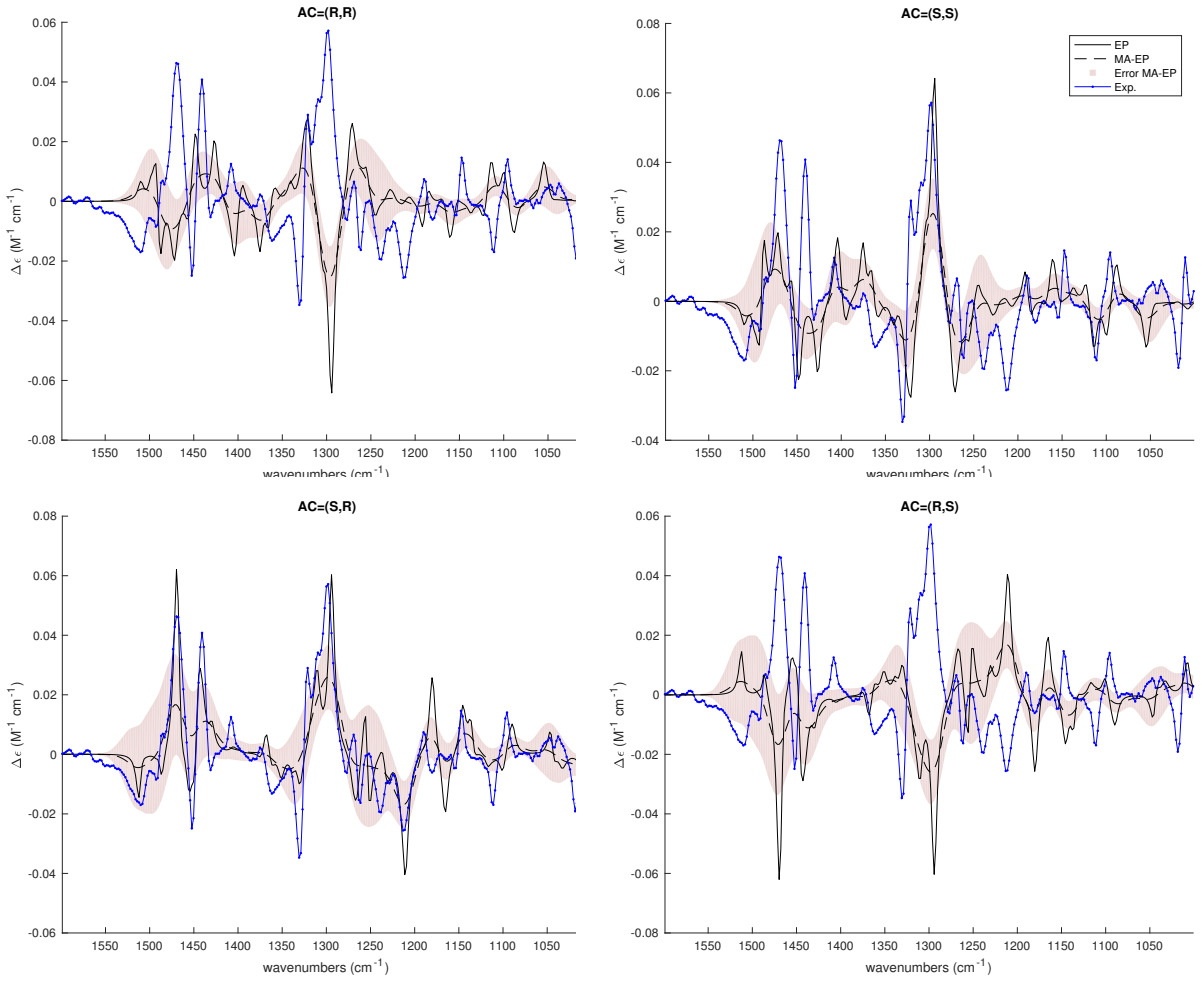

Figure S7: VCD spectrum of (*S*,*R*)-**1** and its fit with EP and MA-EP methods for all 4 possible ACs.

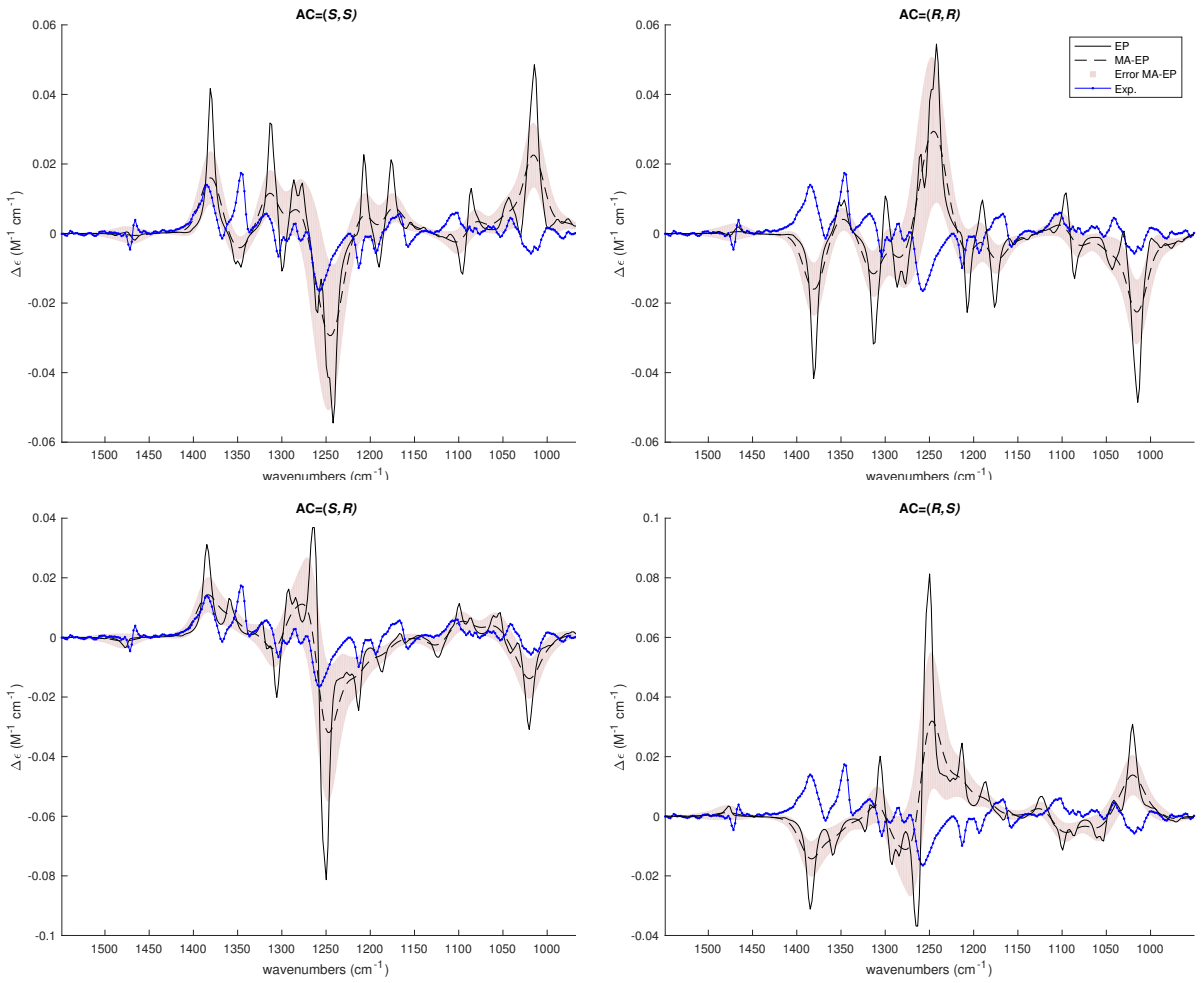

Figure S8: VCD spectrum of (S^*, R^*)-**2** and its fit with EP and MA-EP methods for all 4 possible ACs.

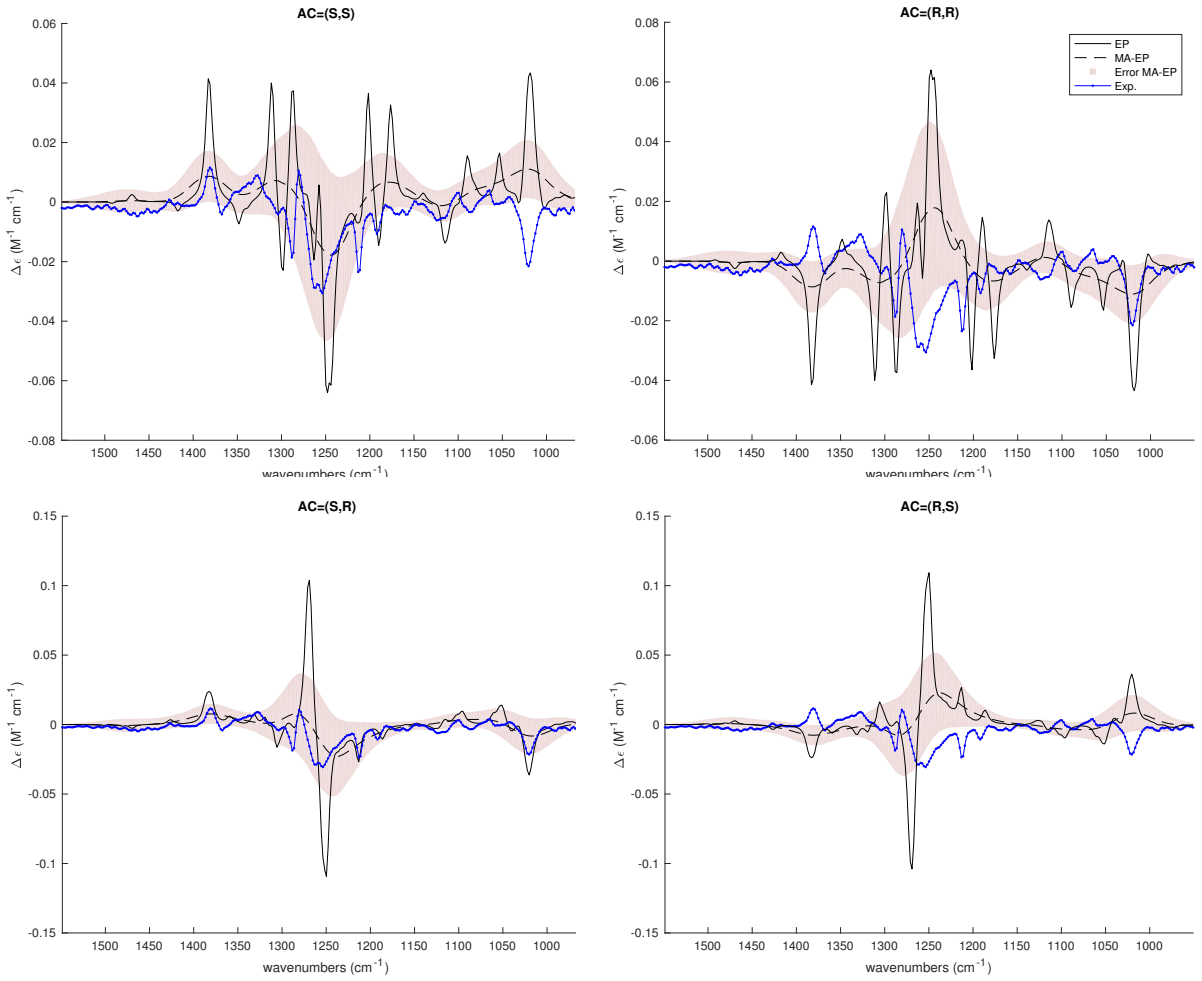

Figure S9: VCD spectrum of (ξ,ξ')-**3** and its fit with EP and MA-EP methods for all 4 possible ACs.

Table S7: GOFIs for the VCD spectrum of (*R*,*R*)-1 in chloroform, calculated using the four possible ACs, conformer populations obtained by energy, enthalpy or free-enthalpy, and either plain SCRF-ω-B97XD/6-31G* calculations or their model-averaged version.

Method	AC	RMSE	MAE	$\cos\theta$	SI	ESI
EP	(*R*,*R*)	4.41	3.25	0.81	0.83	0.83
	(*S*,*S*)	12.91	8.04	-0.81	0.02	0.11
	(*S*,*R*)	12.02	7.29	-0.38	0.15	0.12
	(*R*,*S*)	8.08	5.61	0.38	0.49	0.47
HP	(*R*,*R*)	4.41	3.25	0.81	0.83	0.83
	(*S*,*S*)	12.97	8.07	-0.81	0.02	0.11
	(*S*,*R*)	12.03	7.29	-0.38	0.15	0.12
	(*R*,*S*)	8.07	5.60	0.38	0.49	0.47
GP	(*R*,*R*)	4.44	3.25	0.81	0.83	0.83
	(*S*,*S*)	13.12	8.12	-0.81	0.02	0.10
	(*S*,*R*)	12.05	7.29	-0.39	0.14	0.12
	(*R*,*S*)	8.02	5.58	0.39	0.49	0.48
MA-EP	(*R*,*R*)	1.50	1.10	0.62	0.68	0.65
	(*S*,*S*)	2.38	1.81	-0.62	0.05	0.24
	(*S*,*R*)	2.22	1.64	-0.03	0.30	0.21
	(*R*,*S*)	2.17	1.58	0.03	0.34	0.26
MA-HP	(*R*,*R*)	1.47	1.08	0.62	0.68	0.65
	(*S*,*S*)	2.32	1.76	-0.62	0.05	0.23
	(*S*,*R*)	2.17	1.59	-0.02	0.30	0.21
	(*R*,*S*)	2.12	1.54	0.02	0.34	0.26
MA-GP	(*R*,*R*)	1.22	0.89	0.59	0.66	0.63
	(*S*,*S*)	1.86	1.42	-0.59	0.07	0.22
	(*S*,*R*)	1.73	1.28	0.01	0.31	0.22
	(*R*,*S*)	1.75	1.26	-0.01	0.32	0.24

Table S8: GOFIs for the VCD spectrum of (*S*,*R*)-1 in chloroform, calculated using the four possible ACs, conformer populations obtained by energy, enthalpy or free-enthalpy, and either plain SCRF-ω-B97XD/6-31G* calculations or their model-averaged version.

Method	AC	RMSE	MAE	$\cos\theta$	SI	ESI
EP	(*R*,*R*)	11.26	7.09	-0.45	0.12	0.02
	(*S*,*S*)	7.11	4.96	0.45	0.52	0.49
	(*S*,*R*)	5.11	3.69	0.74	0.74	0.74
	(*R*,*S*)	13.08	8.05	-0.74	0.03	0.05
HP	(*R*,*R*)	11.27	7.09	-0.44	0.12	0.02
	(*S*,*S*)	7.18	5.00	0.44	0.51	0.49
	(*S*,*R*)	5.10	3.69	0.75	0.75	0.74
	(*R*,*S*)	13.09	8.05	-0.75	0.03	0.06
GP	(*R*,*R*)	11.30	7.09	-0.42	0.13	0.04
	(*S*,*S*)	7.37	5.09	0.42	0.50	0.48
	(*S*,*R*)	5.10	3.68	0.74	0.75	0.74
	(*R*,*S*)	13.08	8.04	-0.74	0.03	0.06
MA-EP	(*R*,*R*)	1.85	1.33	-0.38	0.15	0.05
	(*S*,*S*)	1.38	1.06	0.38	0.50	0.44
	(*S*,*R*)	1.13	0.86	0.67	0.71	0.69
	(*R*,*S*)	2.08	1.49	-0.67	0.05	0.17
MA-HP	(*R*,*R*)	1.84	1.32	-0.37	0.15	0.04
	(*S*,*S*)	1.39	1.06	0.37	0.49	0.43
	(*S*,*R*)	1.12	0.85	0.67	0.71	0.69
	(*R*,*S*)	2.08	1.48	-0.67	0.05	0.17
MA-GP	(*R*,*R*)	1.59	1.13	-0.36	0.15	0.04
	(*S*,*S*)	1.20	0.92	0.36	0.49	0.43
	(*S*,*R*)	0.99	0.75	0.65	0.69	0.68
	(*R*,*S*)	1.78	1.26	-0.65	0.06	0.16

Table S9: GOFIs for the VCD spectrum of (ξ,ξ')-3 in chloroform, calculated using the four possible ACs, conformer populations obtained by energy, enthalpy or free-enthalpy, and either plain B3LYP/6-31G* calculations or their model-averaged version.

Method	AC	RMSE	MAE	$\cos\theta$	SI	ESI
EP	(*R*,*R*)	21.14	13.93	0.22	0.48	0.48
	(*S*,*S*)	27.51	15.39	-0.22	0.25	0.22
	(*S*,*R*)	26.09	10.90	0.46	0.60	0.59
	(*R*,*S*)	36.50	18.81	-0.46	0.14	0.11
HP	(*R*,*R*)	20.53	13.68	0.22	0.49	0.48
	(*S*,*S*)	26.90	15.11	-0.22	0.25	0.22
	(*S*,*R*)	26.08	10.87	0.47	0.60	0.59
	(*R*,*S*)	36.62	18.89	-0.47	0.14	0.11
GP	(*R*,*R*)	19.69	13.41	0.22	0.48	0.48
	(*S*,*S*)	26.03	14.45	-0.22	0.25	0.23
	(*S*,*R*)	29.46	11.82	0.50	0.61	0.60
	(*R*,*S*)	40.91	20.45	-0.50	0.12	0.10
MA-EP	(*R*,*R*)	1.36	1.58	-0.15	0.28	0.24
	(*S*,*S*)	1.60	1.36	0.15	0.34	0.31
	(*S*,*R*)	1.22	1.20	0.25	0.48	0.42
	(*R*,*S*)	1.81	1.65	-0.25	0.18	0.14
MA-HP	(*R*,*R*)	1.37	1.60	-0.14	0.28	0.23
	(*S*,*S*)	1.62	1.37	0.14	0.34	0.30
	(*S*,*R*)	1.24	1.21	0.25	0.48	0.42
	(*R*,*S*)	1.84	1.68	-0.25	0.18	0.14
MA-GP	(*R*,*R*)	1.16	1.35	-0.14	0.27	0.21
	(*S*,*S*)	1.37	1.15	0.14	0.33	0.29
	(*S*,*R*)	1.07	1.04	0.24	0.48	0.43
	(*R*,*S*)	1.62	1.45	-0.24	0.17	0.16

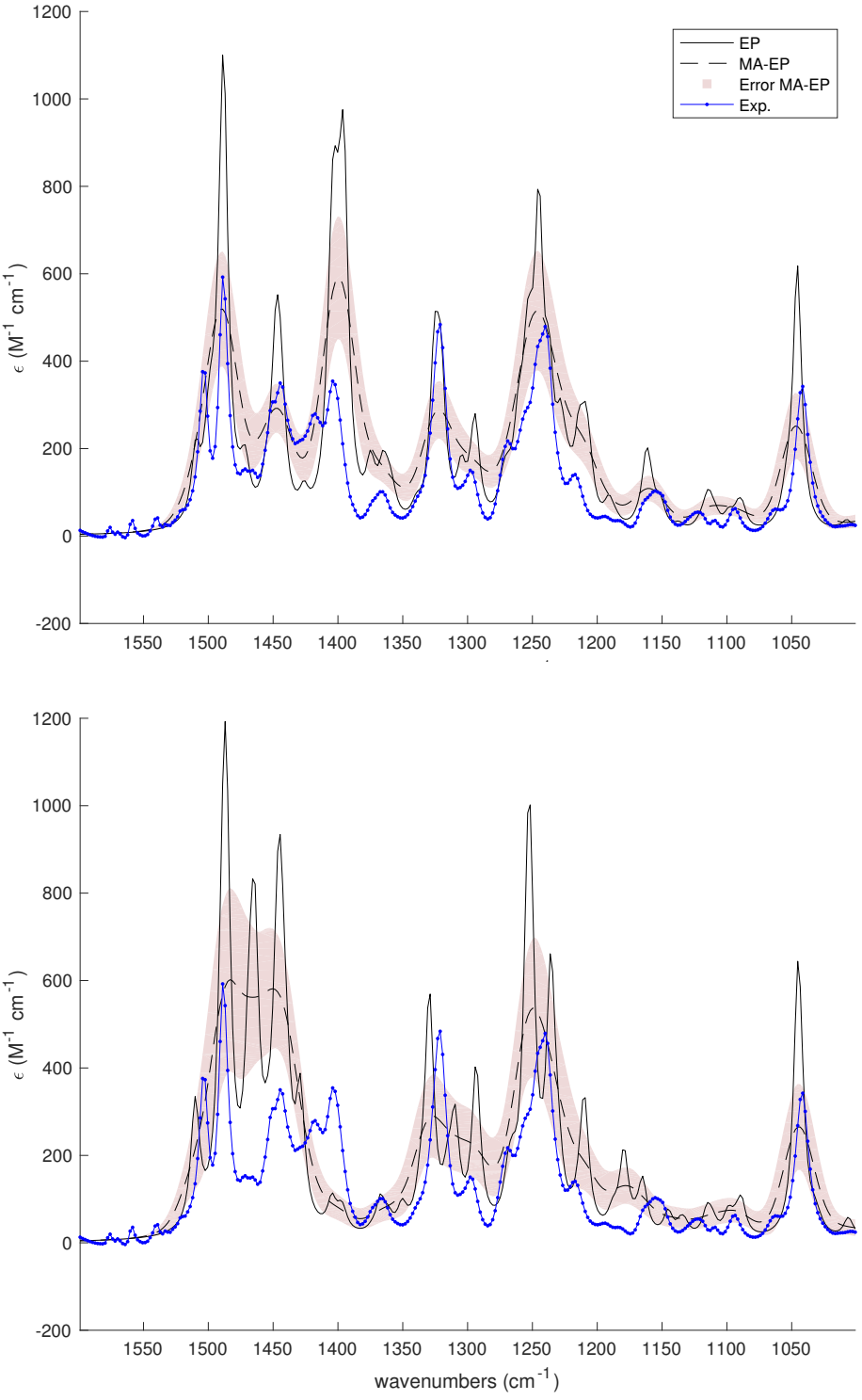

Figure S10: VA spectrum of (*R*,*R*)-**1** and its fit with EP and MA-EP methods. The relative configuration (R^*, R^*) has been used in the upper panel, the relative configuration (R^*, S^*) has been used in the lower panel.

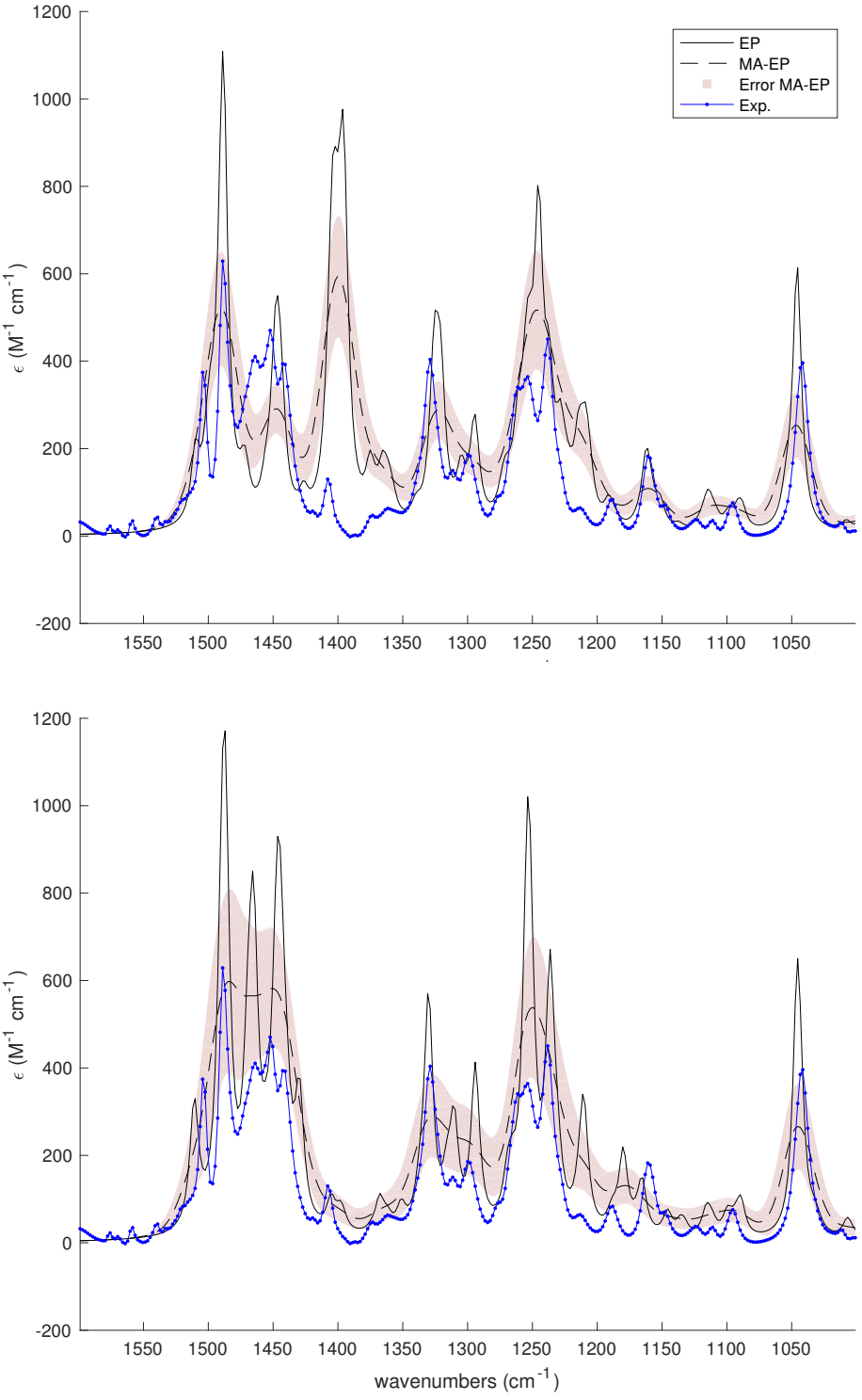

Figure S11: VA spectrum of (*S*,*R*)-**1** and its fit with EP and MA-EP methods. The relative configuration (R^*, R^*) has been used in the upper panel, the relative configuration (R^*, S^*) has been used in the lower panel.

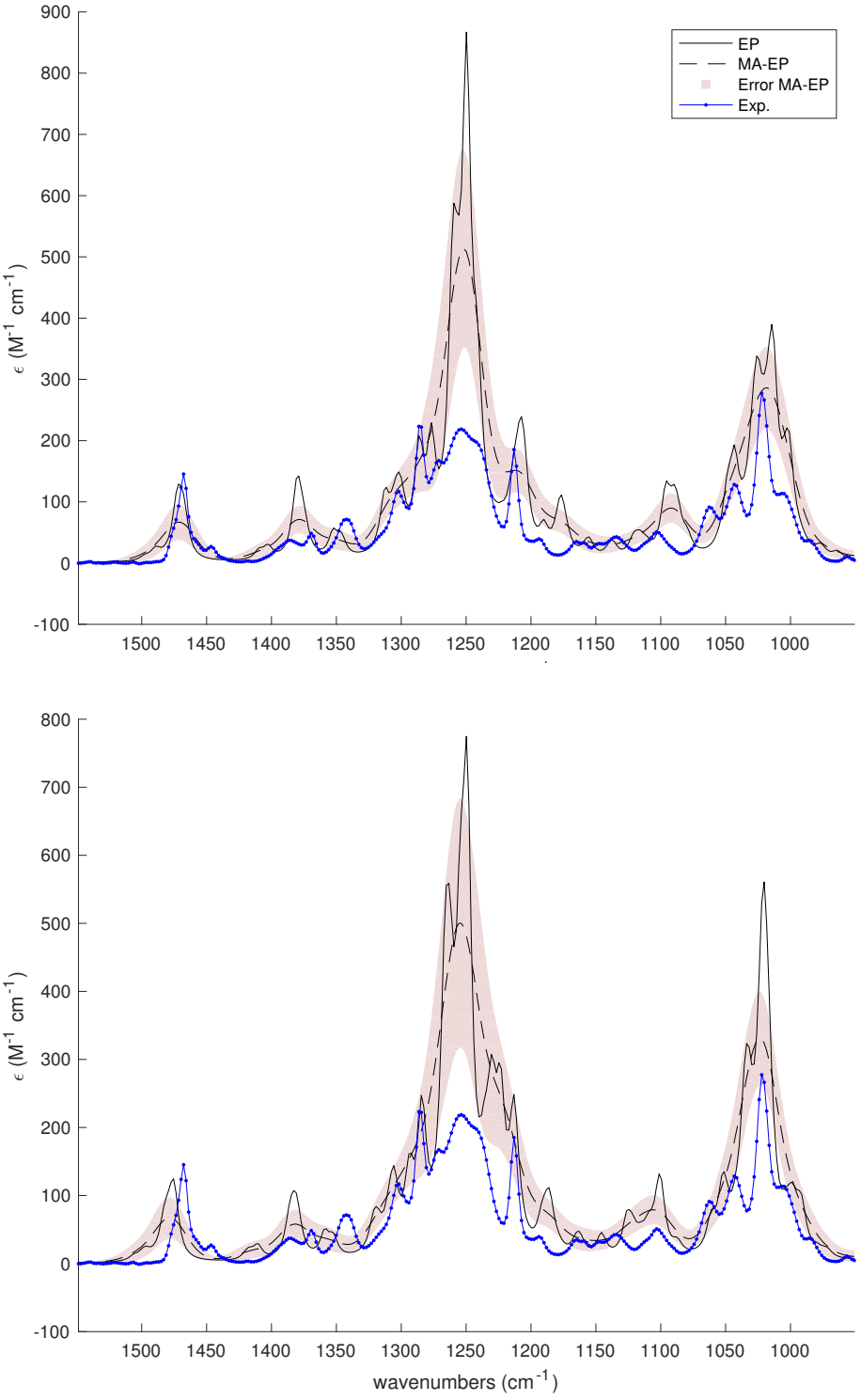

Figure S12: VA spectrum of (R^*, S^*)-**2** and its fit with EP and MA-EP methods. The relative configuration (R^*, R^*) has been used in the upper panel, the relative configuration (R^*, S^*) has been used in the lower panel.

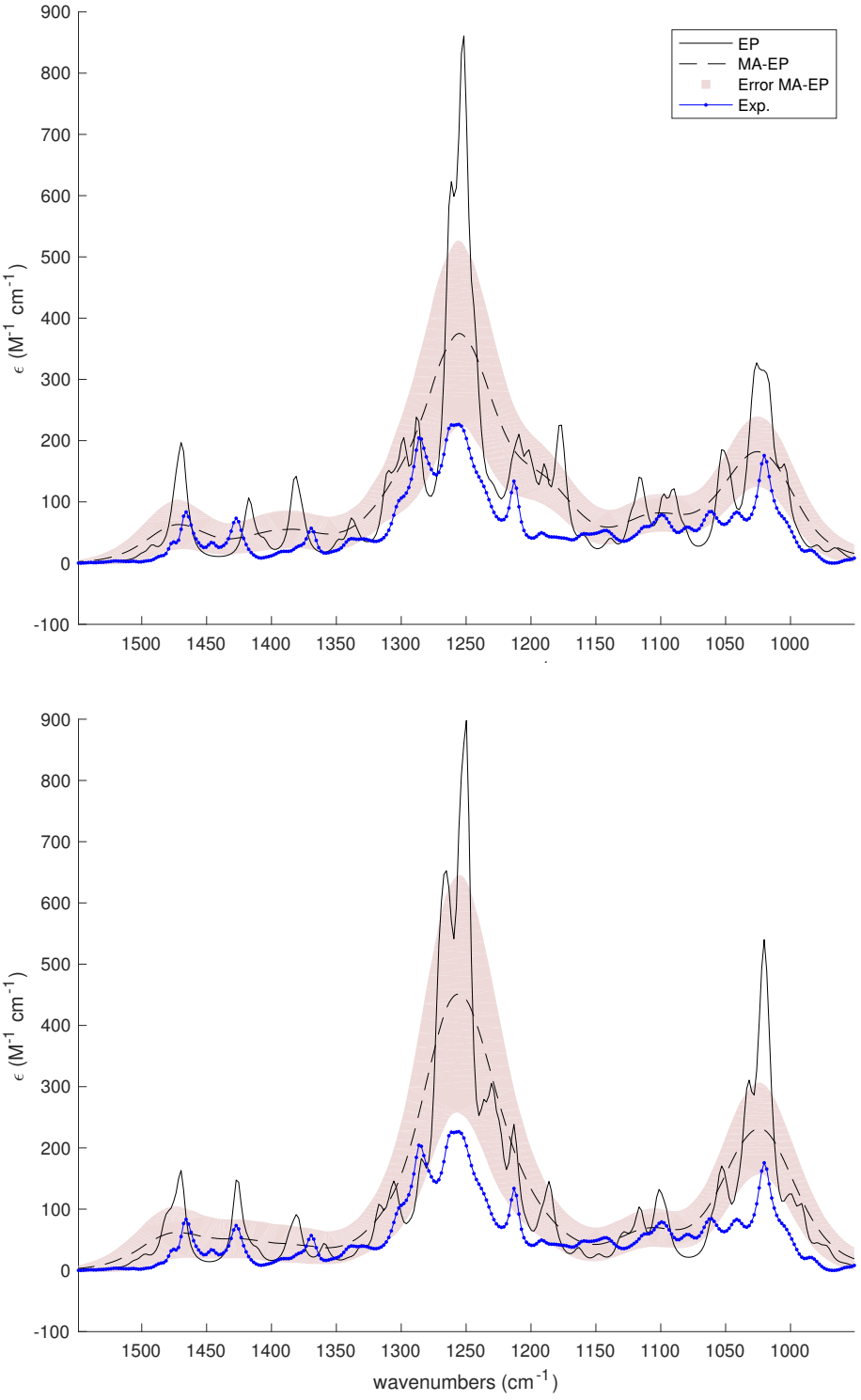

Figure S13: VA spectrum of (ξ,ξ')-**3** and its fit with EP and MA-EP methods. The relative configuration (R^*, R^*) has been used in the upper panel, the relative configuration (R^*, S^*) has been used in the lower panel.

Table S10: GOFIs for the VA spectrum of (*R*,*R*)-1 in chloroform, calculated using the four possible ACs, conformer populations obtained by energy, enthalpy or free-enthalpy, and either plain SCRF-ω-B97XD/6-31G* calculations or their model-averaged version.

method	AC	RMSE	MAE	$\cos\theta$
EP	(R^*, R^*)	13.14	13.53	0.90
	(R^*, S^*)	13.14	13.53	0.84
HP	(R^*, R^*)	13.14	13.53	0.90
	(R^*, S^*)	13.14	13.53	0.83
GP	(R^*, R^*)	13.14	13.53	0.90
	(R^*, S^*)	13.14	13.53	0.83
MA-EP	(R^*, R^*)	1.08	1.23	0.90
	(R^*, S^*)	1.71	1.68	0.87
MA-HP	(R^*, R^*)	1.05	1.20	0.90
	(R^*, S^*)	1.65	1.63	0.88
MA-GP	(R^*, R^*)	0.86	0.97	0.90
	(R^*, S^*)	1.32	1.31	0.87

Table S11: GOFIs for the VA spectrum of (*S*,*R*)-1 in chloroform, calculated using the four possible ACs, conformer populations obtained by energy, enthalpy or free-enthalpy, and either plain SCRF-ω-B97XD/6-31G* calculations or their model-averaged version.

method	AC	RMSE	MAE	$\cos\theta$
EP	(R^*, R^*)	12.81	11.69	0.77
	(R^*, S^*)	12.80	11.69	0.93
HP	(R^*, R^*)	12.81	11.69	0.76
	(R^*, S^*)	12.80	11.69	0.93
GP	(R^*, R^*)	12.81	11.69	0.76
	(R^*, S^*)	12.80	11.69	0.93
MA-EP	(R^*, R^*)	3.53	1.88	0.53
	(R^*, S^*)	0.99	1.20	0.86
MA-HP	(R^*, R^*)	3.52	1.88	0.53
	(R^*, S^*)	0.98	1.20	0.86
MA-GP	(R^*, R^*)	3.01	1.62	0.53
	(R^*, S^*)	0.87	1.04	0.85

Table S12: GOFIs for the VA spectrum of (S^*, R^*)-2 in chloroform, calculated using the four possible ACs, conformer populations obtained by energy, enthalpy or free-enthalpy, and either plain B3LYP/6-31G* calculations or their model-averaged version.

method	AC	RMSE	MAE	$\cos\theta$
EP	(R^*, R^*)	17.62	16.76	0.89
	(S^*, R^*)	17.62	16.76	0.90
HP	(R^*, R^*)	17.62	16.76	0.90
	(S^*, R^*)	17.62	16.76	0.90
GP	(R^*, R^*)	17.62	16.76	0.90
	(S^*, R^*)	17.62	16.76	0.88
MA-EP	(R^*, R^*)	1.07	1.23	0.87
	(S^*, R^*)	1.20	1.37	0.86
MA-HP	(R^*, R^*)	1.06	1.23	0.87
	(S^*, R^*)	1.18	1.36	0.86
MA-GP	(R^*, R^*)	0.82	0.98	0.87
	(S^*, R^*)	0.91	1.08	0.85

Table S13: GOFIs for the VA spectrum of (ξ, ξ')-3 in chloroform, calculated using the four possible ACs, conformer populations obtained by energy, enthalpy or free-enthalpy, and either plain B3LYP/6-31G* calculations or their model-averaged version.

method	AC	RMSE	MAE	$\cos\theta$
EP	(R^*, R^*)	26.35	29.03	0.89
	(R^*, S^*)	26.34	29.03	0.89
HP	(R^*, R^*)	26.35	29.03	0.90
	(R^*, S^*)	26.34	29.03	0.89
GP	(R^*, R^*)	26.35	29.03	0.91
	(R^*, S^*)	26.34	29.03	0.88
MA-EP	(R^*, R^*)	1.00	1.39	0.90
	(R^*, S^*)	1.18	1.43	0.88
MA-HP	(R^*, R^*)	1.01	1.41	0.90
	(R^*, S^*)	1.18	1.43	0.88
MA-GP	(R^*, R^*)	0.79	1.14	0.90
	(R^*, S^*)	0.96	1.15	0.87

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