Aspeterreurone A, a Cytotoxic Dihydrobenzofuran-phenylacrylate Hybrid from the Deep Sea-Derived Fungus *Aspergillus terreus* CC-S06-18

Weiyi Wang[†,▽,*], *Jing Yang*[‡,▽], *Yan-Yan Liao*[⊥], *Gang Cheng*[‡], *Jing Chen*[‡], *Shaowei Mo*[//], *Li Yuan*[//], *Xiang-Dong Cheng*[§,*], *Jiang-Jiang Qin*[‡,§,*], *Zongze Shao*[†]

[†] Key Laboratory of Marine Biogenetic Resources, Third Institute of Oceanography, Ministry of Natural Resources, 184 Daxue Road, Xiamen 361005, PR China

[‡] College of Pharmaceutical Sciences, Zhejiang Chinese Medical University, 548 Binwen Road, Hangzhou 310053, PR China

[//] First Clinical Medical College, Zhejiang Chinese Medical University, 548 Binwen Road, Hangzhou 310053, PR China

[§] Institute of Cancer and Basic Medicine, Chinese Academy of Sciences; Cancer Hospital of the University of Chinese Academy of Sciences; Zhejiang Cancer Hospital, Banshan Road 1#, Hangzhou 310022, PR China

[⊥] Key Laboratory of Urban Environment and Health, Institute of Urban Environment, Chinese Academy of Sciences, 1799 Jimei Road, Xiamen 361021, PR China

Corresponding Authors

*Tel/Fax (W. Wang): +86-592-2195518. Email: wywang@tio.org.cn

*Tel/Fax (X.-D. Cheng): +86-571-87070965. Email: chengxd516@126.com

*Tel/Fax (J.-J. Qin): +86-571-86633013. Email: jqin@zcmu.edu.cn

Table of Content

Computational method

The conformational search was carried out using Spartan'14 (Wavenfunction, Irvine, CA, USA) using the Monte Carlo algorithm and Merck molecular force field (MMFF) with standard parameters and convergence criteria. The conformers within an energy window of 5 kcal/mol were optimized with DFT calculations at M06-2X/def2-SVP level of theory with Grimme's D3 dispersion correction ("EmpiricalDispersion=GD3" key words in input files) using Gaussian 09 program.[1] Frequency analysis of all optimized conformations was undertaken at the same level of theory to ensure they were true local minima on the potential energy surface. Then, energies of all optimized conformations were evaluated by M06-2X/def2-TZVP with D3 dispersion correction. Gibbs free energies of each conformers were calculated by adding "Thermal correction to Gibbs Free Energy" obtained by frequency analysis to electronic energies obtained at M06-2X/def2-TZVP. Room-temperature (298.15 K) equilibrium populations were calculated according to Boltzmann distribution law. Those conformers accounting for over 98% population were subjected to subsequent calculations.

NMR shielding constants were calculated with the GIAO method at mPW1PW91-SCRF/6-31+G(d,p) level with IEFPCM solvent model in acetone solvent. The shielding constants obtained were converted into chemical shifts by referencing to TMS at 0 ppm ($\delta_{cal} = \sigma_{TMS} - \sigma_{cal}$), where the σTMS was the shielding constant of TMS calculated at the same level.[2] The DP4+ probabilities of each possible candidate were calculated with the EXCEL spreadsheet provided by Sarotti *et al*.[3] For each possible candidate, the parameters a and b of the linear regression δcal = $a\delta$exp + b; the correlation coefficient, R^2; the mean absolute error (MAE) defined as $\Sigma n\ |\delta cal - \delta exp|/n$; the corrected mean absolute error, CMAE, defined as $\Sigma n\ |\delta corr - \delta exp|/n$, where $\delta corr = (\delta cal - b)/a$, were calculated.

Time-dependent density-functional theory (TDDFT) ECD calculations were run at CAM-B3LYP/def2-SVP level of theory in MeOH with IEFPCM solvent model, respectively. For each conformer, 30 excited states were calculated.[4] The calculated ECD curves were generated using Multiwfn 3.6 software.[5]

References

(1) Frisch, M. J.; Trucks, G. W.; Schlegel, H. B.; Scuseria, G. E.; Robb, M. A.; Cheeseman, J. R.; Scalmani, G.; Barone, V.; Mennucci, B.; Petersson, G. A.; Nakatsuji, H.; Caricato, M.; Li, X.; Hratchian, H. P.; Izmaylov, A. F.; Bloino, J.; Zheng, G.; Sonnenberg, J. L.; Hada, M.; Ehara, M.; Toyota, K.; Fukuda, R.; Hasegawa, J.; Ishida, M.; Nakajima, T.; Honda, Y.; Kitao, O.; Nakai, H.; Vreven, T.; Montgomery, J. A.; Jr., J. E. P.; Ogliaro, F.; Bearpark, M.; Heyd, J. J.; Brothers, E.; Kudin, K. N.; Staroverov, V. N.; Keith, T.; Kobayashi, R.; Normand, J.; Raghavachari, K.; Rendell, A.; Burant, J. C.; Iyengar, S. S.; Tomasi, J.; Cossi, M.; Rega, N.; Millam, J. M.; Klene, M.; Knox, J. E.; Cross, J. B.; Bakken, V.; Adamo, C.; Jaramillo, J.; Gomperts, R.; Stratmann, R. E.; Yazyev, O.; Austin, A. J.; Cammi, R.; Pomelli, C.; Ochterski, J. W.; Martin, R. L.; Morokuma, K.; Zakrzewski, V. G.; Voth, G. A.; Salvador, P.; Dannenberg, J. J.; Dapprich, S.; Daniels, A. D.; Farkas, O.; Foresman, J. B.; Ortiz, J. V.; Cioslowski, J.; Fox, D. J. Gaussian 16 Rev. C.01, Wallingford CT **2016**.

(2) Willoughby, P. H.; Jansma, M. J.; Hoye, T. R. *Nat. Protoc.* **2014,** *9*, 643-660.

(3) Grimblat, N.; Zanardi, M. M.; Sarotti, A. M. *J. Org. Chem.* **2015**, *80*, 12526-12534.

(4) Pescitelli, G.; Bruhn, T. *Chirality* **2016**, *28*, 466-474.

(5) Lu, T.; Chen, F. *J. Comput. Chem.* **2011**, *33*, 580-592.

Computational data of (2*S**, 3*R**)-a

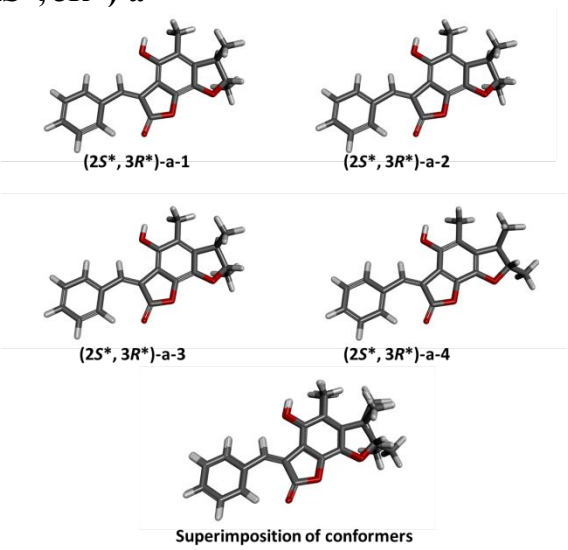


Figure S1. Optimized geometries of 4 dominant conformers of **(2*S**, 3*R**)-a** (**(2*S**, 3*R**)-a-1** to **(2*S**, 3*R**)-a-4**, respectively) at the M06-2X/def2-SVP level of theory in the gas phase

Table S1. Parameters of the M06-2X/def2-SVP optimized conformers of **(2*S**, 3*R**)-a** in the gas phase

Conformers	E [a] (Hartree)	C [b] (Hartree)	G [c] (kcal/mol)
(2*S, 3*R**)-a-1**	-1073.840595	0.2883	-673654.065
(2*S, 3*R**)-a-2**	-1073.840709	0.289404	-673653.4436
(2*S, 3*R**)-a-3**	-1073.840838	0.289948	-673653.1838
(2*S, 3*R**)-a-4**	-1073.838908	0.289286	-673652.3877

[a] Electronic energy obtained at M06-2X/def2-TZVP level of theory; [b] Thermal correction to Gibbs free energy obtained at M06-2X/def2-SVP level of theory; [C] Gibbs free energy (E + C).

Table S2. Conformational analysis of the M06-2X/def2-SVP optimized conformers of **(2*S**, 3*R**)-a**

Conformers	ΔG (kcal/mol) [a]	Population [b]
(2*S, 3*R**)-a-1**	0	61.2%
(2*S, 3*R**)-a-2**	0.621319125	21.4%
(2*S, 3*R**)-a-3**	0.8811857	13.8%
(2*S, 3*R**)-a-4**	1.6772824	3.6%

[a] The relative Gibbs free energy; [b] The Boltzmann distribution of each conformer. (T=298.15 K)

Table S3. Optimized Z-matrixes of **(2*S**, 3*R**)-a-1** in the gas phase (Å) at the M06-2X/def2-SVP level of theory.

C	2.06631	2.05447	2.17493	C	-2.92865	-6.24692	0.80174
C	3.26846	3.42319	-0.93922	C	-2.9635	-5.5445	-0.40293
C	-0.25288	4.81824	-1.55983	C	-2.34645	-4.30267	-0.52392
C	1.78236	3.58561	-0.61286	H	1.44824	2.06204	3.08836
C	0.92951	3.91732	-1.86405	H	2.96315	1.44522	2.37784
C	-0.97594	-2.44897	0.59815	H	2.40457	3.08478	2.01022
C	-1.31924	-1.28029	-1.69353	H	3.83362	3.082	-0.06017
C	-0.05052	-0.20472	-0.03998	H	3.39636	2.67497	-1.73531
C	-0.80334	-1.43593	-0.29003	H	3.70274	4.37407	-1.2819

C	1.29289	1.5402	0.98869	H	0.091	5.81559	-1.25111
C	1.16064	2.27104	-0.19252	H	-0.89018	4.91992	-2.44769
C	0.44623	1.80092	-1.29685	H	-0.85471	4.38598	-0.74613
C	-0.15685	0.56177	-1.20659	H	1.64591	4.36946	0.14911
C	0.66774	0.27985	1.05815	H	1.54697	4.34235	-2.66847
O	-1.98113	-1.99567	-2.38187	H	-0.48492	-2.25792	1.55546
O	0.44003	2.65181	-2.34846	H	1.28828	-0.05634	2.83686
O	0.74163	-0.49173	2.17396	H	-1.12166	-4.0372	2.64253
O	-0.89454	-0.06228	-2.16842	H	-2.22947	-6.24088	2.8467
C	-1.67219	-3.73671	0.57504	H	-3.41686	-7.21936	0.88509
C	-1.64339	-4.46328	1.78297	H	-3.47963	-5.96864	-1.26548
C	-2.26441	-5.70056	1.89967	H	-2.38615	-3.76622	-1.46814

Table S4. Optimized Z-matrixes of **(2*S**, 3*R**)-a-2** in the gas phase (Å) at the M06-2X/def2-SVP level of theory.

C	2.24231	1.84429	2.19619	C	-2.2802	-6.55777	0.01775
C	2.79808	3.86087	-0.76272	C	-2.59228	-5.64985	-0.99416
C	-0.88282	4.94102	-0.53373	C	-2.09532	-4.35013	-0.96605
C	1.38527	3.8073	-0.177	H	1.77266	1.66013	3.17715
C	0.30482	4.2615	-1.19028	H	3.18785	1.2778	2.16143
C	-0.6694	-2.60386	0.25432	H	2.49981	2.9099	2.16151
C	-1.47257	-1.0897	-1.69502	H	3.53299	3.42842	-0.06895
C	-0.03306	-0.19744	-0.07272	H	2.83494	3.28392	-1.69846
C	-0.72413	-1.43624	-0.4378	H	3.09528	4.89738	-0.98029
C	1.32376	1.47029	1.06183	H	-0.58235	5.9007	-0.08994
C	0.94565	2.38004	0.07391	H	-1.67218	5.12196	-1.27474
C	0.09867	2.03884	-0.98351	H	-1.2901	4.29774	0.26081
C	-0.38532	0.74704	-1.04396	H	1.32804	4.42564	0.73279
C	0.81381	0.15947	0.9819	H	0.73397	4.89905	-1.97657
O	-2.18379	-1.73675	-2.40157	H	-0.03773	-2.53814	1.14362
O	-0.14652	3.0575	-1.83943	H	1.7035	-0.40386	2.57925
O	1.12504	-0.78353	1.90895	H	-0.31312	-4.5536	1.92834
O	-1.2208	0.22897	-1.98832	H	-1.20563	-6.85968	1.86889
C	-1.26453	-3.93146	0.09079	H	-2.67597	-7.57417	-0.01527
C	-0.95763	-4.86345	1.10305	H	-3.23365	-5.95576	-1.82198
C	-1.45787	-6.15931	1.07148	H	-2.3495	-3.6551	-1.76147

Table S5. Optimized Z-matrixes of **(2*S**, 3*R**)-a-3** in the gas phase (Å) at the M06-2X/def2-SVP level of theory.

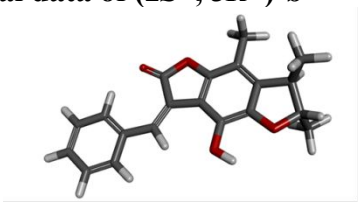
C	2.85582	1.59182	1.59057	C	-2.77166	-6.34428	0.56333
C	2.87043	3.60919	-1.4066	C	-1.66606	-6.0485	1.36037
C	-0.52683	5.03347	-0.32235	C	-1.06943	-4.79706	1.27272
C	1.63556	3.67269	-0.50477	H	2.63103	1.39642	2.65251
C	0.39378	4.24413	-1.23439	H	3.72053	0.9686	1.30701

C	-0.82715	-2.53967	0.41008	H	3.17314	2.63941	1.51995
C	-1.94691	-0.91351	-1.27368	H	3.70286	3.0956	-0.90479
C	-0.07922	-0.18909	-0.05397	H	2.6331	3.05169	-2.3246
C	-0.94781	-1.35369	-0.24082	H	3.20534	4.61833	-1.68827
C	1.65975	1.32566	0.71391	H	-0.03025	5.94938	0.02808
C	1.13736	2.28735	-0.1519	H	-1.44453	5.30888	-0.85801
C	0.03026	2.04698	-0.96891	H	-0.80229	4.42557	0.55284
C	-0.57055	0.80503	-0.90854	H	1.85264	4.27543	0.39147
C	1.02928	0.06701	0.76004	H	0.68398	4.84473	-2.10847
O	-2.86587	-1.47866	-1.78328	H	0.00927	-2.54972	1.11307
O	-0.31958	3.10038	-1.74205	H	2.24716	-0.61943	2.06521
O	1.46986	-0.92056	1.58246	H	-3.0712	-3.38438	-1.09543
O	-1.65557	0.38474	-1.61882	H	-4.13117	-5.60664	-0.94039
C	-1.5562	-3.80919	0.39232	H	-3.24671	-7.32467	0.62694
C	-2.67276	-4.12409	-0.4061	H	-1.26907	-6.79378	2.05107
C	-3.26669	-5.37961	-0.31467	H	-0.20367	-4.56597	1.89691

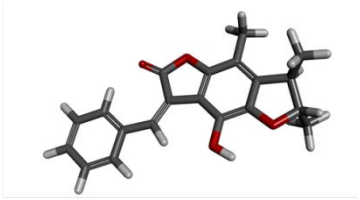
Table S6. Optimized Z-matrixes of **(2*S**, 3*R**)-a-4** in the gas phase (Å) at the M06-2X/def2-SVP level of theory.

C	2.81317	1.51964	1.60776	C	-2.98844	-6.32813	0.84839
C	3.03817	3.76252	-0.86814	C	-1.85709	-6.04203	1.61219
C	0.05183	5.36995	-1.58787	C	-1.23107	-4.80905	1.47964
C	1.57149	3.60137	-0.47326	H	2.67935	1.07473	2.60684
C	0.63447	3.97736	-1.65368	H	3.75913	1.13897	1.18812
C	-0.95371	-2.57922	0.55887	H	2.93313	2.59819	1.76719
C	-2.0994	-0.94737	-1.10136	H	3.72148	3.59214	-0.02661
C	-0.16946	-0.25238	0.03561	H	3.2967	3.0539	-1.66869
C	-1.06906	-1.39998	-0.10506	H	3.22096	4.78185	-1.24143
C	1.62628	1.23715	0.72148	H	0.85744	6.1183	-1.60022
C	1.11382	2.18941	-0.16514	H	-0.60954	5.55277	-2.44479
C	-0.04149	1.96629	-0.9176	H	-0.53088	5.48934	-0.66359
C	-0.66947	0.74054	-0.81222	H	1.35092	4.25402	0.39206
C	0.98066	-0.01281	0.79593	H	1.19697	3.84551	-2.59675
O	-3.05005	-1.49697	-1.56794	H	-0.09415	-2.59856	1.23297
O	-0.43176	3.01846	-1.66894	H	2.27474	-0.75745	1.99341
O	1.42874	-1.007	1.60697	H	-3.25244	-3.40181	-0.87509
O	-1.79429	0.341	-1.47065	H	-4.36309	-5.59276	-0.64254
C	-1.7141	-3.82991	0.58747	H	-3.48637	-7.29419	0.94693
C	-2.85625	-4.13527	-0.17781	H	-1.46284	-6.78055	2.31168
C	-3.47917	-5.37265	-0.04203	H	-0.34533	-4.58531	2.07791

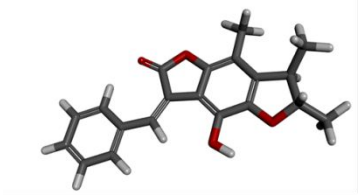
Computational data of (2*S**, 3*R**)-b



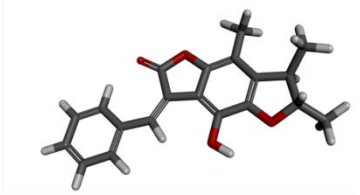
(2*S**, 3*R**)-b-1



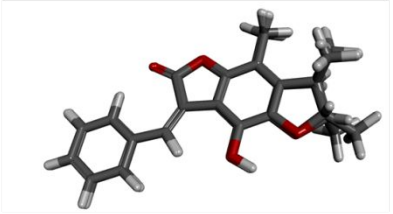
(2*S**, 3*R**)-b-2



(2*S**, 3*R**)-b-3



(2*S**, 3*R**)-b-4



Superimposition of conformers

Figure S2. Optimized geometries of 4 dominant conformers of **(2*S**, 3*R**)-b** ((**2*S**, 3*R**)-b-1** to **(2*S**, 3*R**)-b -4**, respectively) at the M06-2X/def2-SVP level of theory in the gas phase

Table S7. Parameters of the M06-2X/def2-SVP optimized conformers of **(2*S**, 3*R**)-b** in the gas phase

Conformers	E [a] (Hartree)	C [b] (Hartree)	G [c] (kcal/mol)
(2*S, 3*R**)-b-1**	-1073.848922	0.288743	-673659.0122
(2*S, 3*R**)-b-2**	-1073.848912	0.289113	-673658.7741
(2*S, 3*R**)-b-3**	-1073.848283	0.288983	-673658.4607
(2*S, 3*R**)-b-4**	-1073.848224	0.289504	-673658.0965

[a] Electronic energy obtained at M06-2X/def2-TZVP level of theory; [b] Thermal correction to Gibbs free energy obtained at M06-2X/def2-SVP level of theory; [C] Gibbs free energy (E + C).

Table S8. Conformational analysis of the M06-2X/def2-SVP optimized conformers of **(2*S**, 3*R**)-b**

Conformers	ΔG (kcal/mol) [a]	Population [b]
(2*S, 3*R**)-b-1**	0	43.9%
(2*S, 3*R**)-b-2**	0.238067225	29.4%
(2*S, 3*R**)-b-3**	0.551553675	17.3%
(2*S, 3*R**)-b-4**	0.91571075	9.4%

[a] The relative Gibbs free energy; [b] The Boltzmann distribution of each conformer. (T=298.15 K)

Table S9. Optimized Z-matrixes of **(2*S**, 3*R**)-b-1** in the gas phase (Å) at the M06-2X/def2-SVP level of theory.

C	-3.47144	-1.60934	-0.38024	C	2.4994	5.4837	3.42517
C	-1.94605	-2.76062	-3.47992	C	1.14467	5.15296	3.46692
C	0.67447	-4.67766	-1.4383	C	0.65476	4.05882	2.7601

C	-1.2501	-3.15839	-2.17743	H	-3.64012	-2.66909	-0.61382
C	0.22946	-3.57833	-2.38397	H	-3.84673	-1.40747	0.63161
C	1.15449	2.09634	1.19435	H	-4.07612	-1.00813	-1.0768
C	-1.38744	1.6418	1.50997	H	-2.95671	-2.37617	-3.28332
C	-0.12948	0.23867	0.11982	H	-1.37415	-1.96826	-3.9852
C	-0.00086	1.4171	0.97521	H	-2.02953	-3.61982	-4.16162
C	-2.01442	-1.25892	-0.48544	H	1.7523	-4.85972	-1.54128
C	-1.08359	-1.97423	-1.24937	H	0.46433	-4.38587	-0.39818
C	0.24879	-1.58938	-1.32901	H	0.1358	-5.61093	-1.6548
C	0.77766	-0.49086	-0.65376	H	-1.80337	-3.97926	-1.69371
C	-1.46996	-0.16487	0.17718	H	0.42473	-3.85786	-3.42935
O	-1.83232	2.46861	2.24733	H	2.00435	1.66673	0.65613
O	1.01075	-2.39185	-2.12434	H	3.57728	3.01355	1.35749
O	-2.19956	0.6641	0.99233	H	4.43748	4.95876	2.6243
O	2.0845	-0.15999	-0.74309	H	2.871	6.34366	3.98493
C	1.52675	3.26797	1.98773	H	0.45591	5.756	4.06042
C	2.89179	3.61821	1.95507	H	-0.40296	3.81227	2.80313
C	3.37606	4.7102	2.66459	H	2.51816	-0.81241	-1.31082

Table S10. Optimized Z-matrixes of **(2*S**, 3*R**)-b-2** in the gas phase (Å) at the M06-2X/def2-SVP level of theory

C	-3.50035	-1.24063	-1.00426	C	2.5046	5.79947	2.85476
C	-1.48954	-3.25725	-3.27795	C	3.39234	4.77813	2.51724
C	0.18423	-4.92258	-0.25539	C	2.91239	3.61608	1.92596
C	-1.21138	-3.4113	-1.78174	H	-3.79813	-2.29786	-0.98446
C	0.17827	-4.03536	-1.48605	H	-4.06832	-0.69955	-0.23645
C	1.17394	2.16961	1.03308	H	-3.79397	-0.82572	-1.98107
C	-1.40807	2.09611	0.72655	H	-2.43302	-2.72053	-3.44933
C	-0.11203	0.27651	0.02486	H	-0.68056	-2.68361	-3.75396
C	0.00673	1.59622	0.64196	H	-1.55737	-4.23899	-3.76961
C	-2.02357	-1.09228	-0.77215	H	1.20746	-5.24272	-0.01854
C	-1.07292	-2.06837	-1.09727	H	-0.22068	-4.37127	0.60673
C	0.28455	-1.86926	-0.88144	H	-0.43564	-5.81458	-0.42295
C	0.81548	-0.71224	-0.31381	H	-1.99947	-4.02504	-1.3168
C	-1.47576	0.05534	-0.21066	H	0.56961	-4.57564	-2.36023
O	-1.86881	3.11464	1.14543	H	2.04212	1.53411	0.83593
O	1.0663	-2.91874	-1.26227	H	-0.40787	4.37334	1.81233
O	-2.2267	1.12832	0.20064	H	0.44448	6.44037	2.85754
O	2.14191	-0.56511	-0.10379	H	2.87406	6.71605	3.3177
C	1.53941	3.44068	1.65932	H	4.45963	4.88856	2.71374
C	0.65619	4.48085	2.00601	H	3.60792	2.8174	1.65981
C	1.14251	5.64372	2.59607	H	2.58004	-1.3769	-0.39547

Table S11. Optimized Z-matrixes of **(2*S**, 3*R**)-b-3** in the gas phase (Å) at the M06-2X/def2-SVP level of theory

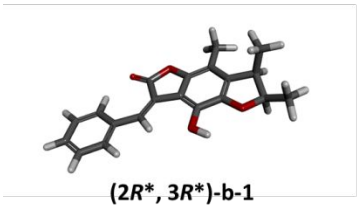
C	-3.49245	-1.26421	-0.73986	C	2.47778	5.38938	3.78198
C	-2.16059	-3.06579	-3.24374	C	1.10778	5.15557	3.66017
C	0.7704	-4.74739	-2.61778	C	0.63032	4.07641	2.92262
C	-1.17349	-3.13022	-2.08236	H	-3.74972	-2.32657	-0.62164
C	0.28418	-3.31803	-2.57696	H	-4.01074	-0.69146	0.03886
C	1.17465	2.03078	1.48273	H	-3.87957	-0.93063	-1.71481
C	-1.41757	1.83301	1.3902	H	-3.19954	-3.02567	-2.89303
C	-0.10127	0.25664	0.26694	H	-1.97022	-2.17435	-3.85961
C	0.00694	1.45194	1.10099	H	-2.06068	-3.95506	-3.88471
C	-2.00725	-1.05435	-0.63685	H	1.81008	-4.7957	-2.96764
C	-1.04441	-1.87466	-1.24373	H	0.71569	-5.19095	-1.61358
C	0.31507	-1.64543	-1.07232	H	0.14567	-5.34017	-3.30102
C	0.8375	-0.58426	-0.33423	H	-1.44437	-3.97556	-1.42226
C	-1.46788	-0.00393	0.09619	H	0.37145	-2.85323	-3.57724
O	-1.88957	2.72545	2.02732	H	2.05244	1.5023	1.09951
O	1.12002	-2.55648	-1.68782	H	3.62011	2.77978	1.93224
O	-2.23079	0.92446	0.7611	H	4.45598	4.70364	3.24473
O	2.16896	-0.39542	-0.20659	H	2.83897	6.23921	4.36352
C	1.53054	3.20073	2.28622	H	0.39601	5.82445	4.1463
C	2.91103	3.45197	2.42006	H	-0.43983	3.90724	2.8366
C	3.38241	4.53132	3.15701	H	2.61602	-1.0848	-0.71754

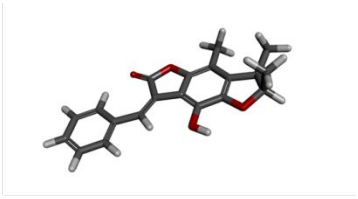
Table S12. Optimized Z-matrixes of **(2*S**, 3*R**)-b-4** in the gas phase (Å) at the M06-2X/def2-SVP level of theory

C	-3.47518	-1.01338	-1.11543	C	2.47278	5.37991	3.80338
C	-2.03692	-3.12761	-3.2911	C	3.3681	4.4268	3.31803
C	0.66161	-4.95154	-2.22952	C	2.89593	3.35949	2.56435
C	-1.18874	-3.15842	-2.0234	H	-3.84479	-2.02948	-0.91502
C	0.29375	-3.49052	-2.33344	H	-4.02823	-0.31049	-0.48078
C	1.16665	2.03952	1.47936	H	-3.70638	-0.77348	-2.16438
C	-1.40135	2.05287	1.06736	H	-3.10352	-3.00105	-3.06676
C	-0.10609	0.30361	0.20683	H	-1.72181	-2.30089	-3.94498
C	0.00735	1.53738	0.9819	H	-1.92508	-4.06989	-3.84876
C	-2.00025	-0.91298	-0.84155	H	1.72532	-5.10292	-2.45569
C	-1.04862	-1.85098	-1.2698	H	0.4628	-5.31668	-1.21214
C	0.29668	-1.71727	-0.94948	H	0.06748	-5.54281	-2.94077
C	0.81975	-0.64999	-0.22089	H	-1.59383	-3.92331	-1.33428
C	-1.46084	0.14195	-0.11491	H	0.52785	-3.10452	-3.34365
O	-1.86381	3.02408	1.58508	H	2.03419	1.42085	1.23215
O	1.08494	-2.7328	-1.40165	H	-0.42966	4.10198	2.55973
O	-2.21145	1.17298	0.39492	H	0.40719	5.99541	3.90334

O	2.13802	-0.55716	0.05798	H	2.8345	6.22025	4.39821
C	1.52422	3.21496	2.27403	H	4.43483	4.51542	3.52812
C	0.6335	4.1868	2.76914	H	3.59728	2.61265	2.18632
C	1.11152	5.25286	3.52522	H	2.58035	-1.32162	-0.33709

Computational data of (2*R**, 3*R**)-b





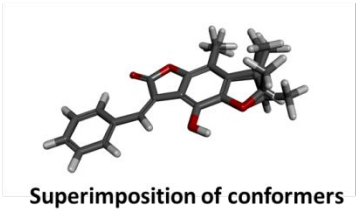


Figure S3. Optimized geometries of 2 dominant conformers of **(2*R**, 3*R**)-b** ((**2*R**, 3*R**)-b-1** to **(2*S**, 3*R**)-b -2**, respectively) at the M06-2X/def2-SVP level of theory in the gas phase

Table S13. Parameters of the M06-2X/def2-SVP optimized conformers of **(2*R**, 3*R**)-b** in the gas phase

Conformers	E [a] (Hartree)	C [b] (Hartree)	G [c] (kcal/mol)
(2*R, 3*R**)-b-1**	-1073.848109	0.28933	-673658.134
(2*R, 3*R**)-b-2**	-1073.846138	0.290614	-673656.0914

[a] Electronic energy obtained at M06-2X/def2-TZVP level of theory; [b] Thermal correction to Gibbs free energy obtained at M06-2X/def2-SVP level of theory; [C] Gibbs free energy (E + C).

Table S14. Conformational analysis of the M06-2X/def2-SVP optimized conformers of **(2*S**, 3*R**)-b**

Conformers	ΔG (kcal/mol) [a]	Population [b]
(2*R, 3*R**)-b-1**	0	96.9%
(2*R, 3*R**)-b-2**	2.042644275	3.1%

[a] The relative Gibbs free energy; [b] The Boltzmann distribution of each conformer. (T=298.15 K)

Table S15. Optimized Z-matrixes of **(2*R**, 3*R**)-b-1** in the gas phase (Å) at the M06-2X/def2-SVP level of theory

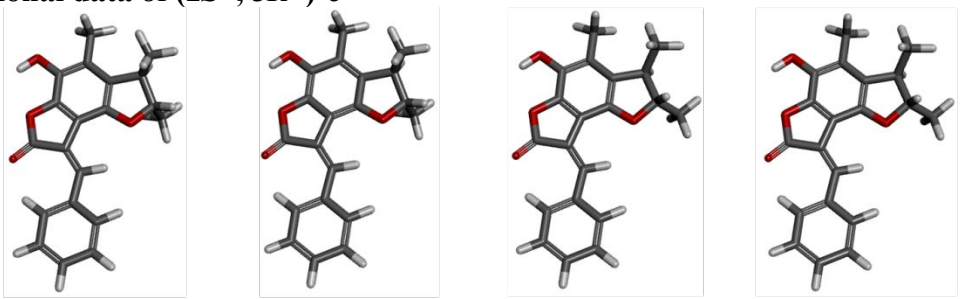
C	-3.74303	0.66063	-0.61436	C	3.47926	-3.19436	5.16337
C	-2.13723	3.18089	-2.70831	C	2.08677	-3.11146	5.18061
C	-0.19651	2.57134	-4.87986	C	1.39449	-2.5081	4.13488
C	-1.86209	1.71567	-3.05261	H	-4.20144	0.77081	-1.60629
C	-0.59402	1.47948	-3.91622	H	-4.19438	-0.20477	-0.11156
C	1.50343	-1.30953	1.87553	H	-4.00117	1.55174	-0.02118
C	-1.07267	-1.1762	2.209	H	-2.98186	3.25225	-2.00884
C	-0.11544	-0.28935	0.26506	H	-1.26018	3.63404	-2.22295
C	0.24008	-0.97672	1.50508	H	-2.38472	3.76807	-3.60439

C	-2.25409	0.49428	-0.72365	H	-0.99435	2.73718	-5.61747
C	-1.4885	0.92943	-1.81229	H	-0.00368	3.51179	-4.3471
C	-0.10733	0.77444	-1.84473	H	0.71711	2.28448	-5.41722
C	0.626	0.16086	-0.83124	H	-2.73575	1.28567	-3.56577
C	-1.50529	-0.11369	0.27787	H	-0.72933	0.52575	-4.45746
O	-1.34731	-1.69055	3.25057	H	2.2526	-1.00912	1.13725
O	0.47691	1.26916	-2.97319	H	4.05779	-1.65572	2.1906
O	-2.05731	-0.63167	1.42289	H	5.27743	-2.72791	4.05852
O	1.96697	0.01559	-0.90863	H	4.01041	-3.6704	5.98934
C	2.09587	-1.97067	3.03884	H	1.52742	-3.52359	6.02183
C	3.50214	-2.0669	3.0361	H	0.30962	-2.44989	4.1635
C	4.18852	-2.66836	4.08387	H	2.25487	0.37536	-1.75936

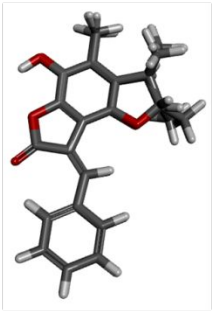
Table S16. Optimized Z-matrixes of **(2*R**, 3*R**)-b-2** in the gas phase (Å) at the M06-2X/def2-SVP level of theory

C	-3.69344	0.60451	-0.65138	C	3.68313	-2.65598	5.28791
C	-2.96214	2.19374	-3.44689	C	2.31351	-2.41121	5.3906
C	-0.14728	2.92207	-3.83506	C	1.59109	-1.92903	4.30328
C	-1.91342	1.08929	-3.36886	H	-4.24904	0.09557	-1.4527
C	-0.53644	1.46199	-3.98927	H	-4.03443	0.20581	0.31149
C	1.60899	-1.17495	1.85706	H	-3.95507	1.67222	-0.68881
C	-0.92902	-0.82278	2.30537	H	-3.94129	1.82779	-3.11439
C	-0.05436	-0.33038	0.1913	H	-2.68971	3.05241	-2.81702
C	0.34551	-0.81895	1.50927	H	-3.07716	2.54765	-4.48216
C	-2.21182	0.39616	-0.80466	H	-0.80697	3.57599	-4.42088
C	-1.48817	0.63813	-1.98254	H	-0.1995	3.22364	-2.77814
C	-0.12352	0.38821	-2.05772	H	0.88312	3.06277	-4.18723
C	0.64154	-0.08842	-0.99496	H	-2.29803	0.20275	-3.90455
C	-1.43224	-0.07976	0.24408	H	-0.48011	1.16057	-5.04417
O	-1.16139	-1.13044	3.43532	H	2.32197	-1.05805	1.03592
O	0.42609	0.65829	-3.2764	H	4.13605	-1.74453	2.04709
O	-1.93507	-0.37386	1.48819	H	5.4092	-2.60232	3.98796
O	1.96958	-0.30303	-1.11447	H	4.23904	-3.03374	6.14766
C	2.23804	-1.68045	3.07778	H	1.7963	-2.59813	6.33285
C	3.62212	-1.93315	2.99201	H	0.52436	-1.74378	4.39794
C	4.33857	-2.41496	4.08057	H	2.23142	-0.05169	-2.01139

Computational data of (2*S**, 3*R**)-c



(2*S**, 3*R**)-c-1 (2*S**, 3*R**)-c-2 (2*S**, 3*R**)-c-3 (2*S**, 3*R**)-c-4



Superimposition of conformers

Figure S4. Optimized geometries of 4 dominant conformers of **(2*S**, 3*R**)-c** (**(2*S**, 3*R**)-c-1** to **(2*S**, 3*R**)-c-4**, respectively) at the M06-2X/def2-SVP level of theory in the gas phase

Table S17. Parameters of the M06-2X/def2-SVP optimized conformers of **(2*S**, 3*R**)-c** in the gas phase

Conformers	E [a] (Hartree)	C [b] (Hartree)	G [c] (kcal/mol)
(2*S, 3*R**)-c-1**	-1073.847658	0.289297	-673657.8717
(2*S, 3*R**)-c-2**	-1073.847597	0.289237	-673657.8708
(2*S, 3*R**)-c-3**	-1073.846108	0.28776	-673657.8634
(2*S, 3*R**)-c-4**	-1073.846235	0.288966	-673657.1864

[a] Electronic energy obtained at M06-2X/def2-TZVP level of theory; [b] Thermal correction to Gibbs free energy obtained at M06-2X/def2-SVP level of theory; [C] Gibbs free energy (E + C).

Table S18. Conformational analysis of the M06-2X/def2-SVP optimized conformers of **(2*S**, 3*R**)-c**

Conformers	ΔG (kcal/mol) [a]	Population [b]
(2*S, 3*R**)-c-1**	0	30.3%
(2*S, 3*R**)-c-2**	0.0008785	30.3%
(2*S, 3*R**)-c-3**	0.008226525	29.9%
(2*S, 3*R**)-c-4**	0.68524255	9.5%

[a] The relative Gibbs free energy; [b] The Boltzmann distribution of each conformer. (T=298.15 K)

Table S19. Optimized Z-matrixes of **(2*S**, 3*R**)-c-1** in the gas phase (Å) at the M06-2X/def2-SVP level of theory

C	-4.63795	-0.07136	0.94995	C	5.39776	2.4963	0.22076
C	-3.35758	-1.67392	-2.01075	C	4.03725	2.25249	0.382
C	-0.82986	-3.57822	0.14679	O	-0.57352	2.6489	1.60347
C	-2.64304	-1.9741	-0.69196	H	-4.9297	0.11809	1.99238

C	-1.21853	-2.54956	-0.89766	H	-5.22931	0.61694	0.32623
C	-3.16668	0.17028	0.76572	H	-4.91106	-1.10063	0.68456
O	-0.32032	-1.42281	-0.79365	H	-4.31607	-1.16691	-1.83137
C	-1.24447	1.55466	1.11814	H	-2.73636	-1.01252	-2.63284
O	-3.3856	2.21062	1.99204	H	-3.55528	-2.59821	-2.57376
C	-2.32826	-0.70852	0.07712	H	-1.45439	-4.47755	0.05136
C	-0.96423	-0.45974	-0.09339	H	0.22356	-3.86446	0.0295
C	-0.39108	0.68987	0.43176	H	-0.96971	-3.1596	1.15491
C	-2.59959	1.34103	1.31029	H	-3.24199	-2.67908	-0.09378
C	2.04295	0.72697	-0.09037	H	-1.09208	-2.9555	-1.91175
C	0.76016	2.55439	1.25723	H	-2.83865	2.94028	2.31115
C	0.94176	1.28039	0.47914	H	1.81944	-0.21919	-0.5957
O	1.52517	3.40816	1.58465	H	3.83648	-0.67336	-1.3513
C	3.45244	1.10357	-0.18378	H	6.25536	-0.22667	-1.63377
C	4.2788	0.22128	-0.90797	H	7.26729	1.81398	-0.62046
C	5.63662	0.47019	-1.06678	H	5.83548	3.391	0.66584
C	6.2016	1.61262	-0.50008	H	3.42317	2.94992	0.94617

Table S20. Optimized Z-matrixes of **(2*S**, 3*R**)-c-2** in the gas phase (Å) at the M06-2X/def2-SVP level of theory

C	-4.66586	-0.06201	0.80355	C	5.67337	0.44709	-0.87118
C	-3.25605	-1.96964	-1.91232	C	4.31419	0.19011	-0.73941
C	-0.76972	-3.55704	0.52918	O	-0.67893	2.807	1.25271
C	-2.58213	-2.09882	-0.54511	H	-4.98059	0.17994	1.82864
C	-1.14104	-2.6626	-0.6384	H	-5.25237	0.58518	0.1334
C	-3.19446	0.1888	0.63409	H	-4.92165	-1.10755	0.59049
O	-0.26709	-1.5118	-0.63577	H	-4.23489	-1.47746	-1.82344
C	-1.31225	1.64896	0.87793	H	-2.6311	-1.3608	-2.5824
O	-3.49268	2.35174	1.60637	H	-3.40577	-2.95654	-2.37511
C	-2.31718	-0.74599	0.08045	H	-1.37462	-4.47464	0.51689
C	-0.95314	-0.48773	-0.07641	H	0.29217	-3.83175	0.48023
C	-0.42021	0.7293	0.32422	H	-0.95235	-3.02988	1.4777
C	-2.66821	1.42791	1.05366	H	-3.18738	-2.74407	0.11128
C	2.03165	0.75667	-0.11073	H	-0.97306	-3.17802	-1.59507
C	0.6668	2.70355	0.96057	H	-2.97169	3.12818	1.84952
C	0.89911	1.35124	0.34459	H	1.84559	-0.24995	-0.50157
O	1.40385	3.6076	1.2076	H	3.31702	3.14564	0.63294
C	3.43705	1.15019	-0.19599	H	5.73103	3.60305	0.39857
C	3.97177	2.38698	0.2119	H	7.25472	1.88508	-0.56264
C	5.33345	2.63941	0.07665	H	6.33315	-0.31202	-1.29355
C	6.18828	1.67704	-0.46197	H	3.9113	-0.77235	-1.06205

Table S21. Optimized Z-matrixes of **(2*S**, 3*R**)-c-3** in the gas phase (Å) at the M06-2X/def2-SVP level of theory

C	-4.65853	0.09847	0.7389	C	5.73522	0.38385	-0.62142
C	-3.62407	-2.22375	-1.45569	C	4.3685	0.15408	-0.52165
C	-0.69865	-3.83376	-0.35526	O	-0.64255	2.94003	1.17124
C	-2.56718	-2.05167	-0.36651	H	-5.06399	0.73402	1.53548
C	-1.16243	-2.48899	-0.8669	H	-5.21008	0.33781	-0.18411
C	-3.18373	0.34295	0.57448	H	-4.85647	-0.9529	0.98824
O	-0.22711	-1.47684	-0.44944	H	-4.63019	-1.9803	-1.09129
C	-1.28243	1.7761	0.82725	H	-3.40097	-1.5689	-2.31102
O	-3.46706	2.56975	1.41882	H	-3.6405	-3.26473	-1.81361
C	-2.30617	-0.6285	0.08055	H	-1.38946	-4.62156	-0.68871
C	-0.93007	-0.40978	-0.00861	H	0.3062	-4.06863	-0.73059
C	-0.38811	0.81361	0.36219	H	-0.672	-3.82847	0.74361
C	-2.65119	1.59455	0.94592	H	-2.84935	-2.66522	0.50893
C	2.08026	0.77428	0.02991	H	-1.16064	-2.48138	-1.97143
C	0.71312	2.7944	0.95125	H	-2.92794	3.33578	1.65518
C	0.94268	1.40885	0.41302	H	1.89007	-0.24581	-0.3217
O	1.45819	3.69368	1.19124	H	3.38928	3.154	0.76438
C	3.49448	1.14085	-0.02296	H	5.81723	3.56134	0.59172
C	4.04092	2.37522	0.37668	H	7.33406	1.79881	-0.29585
C	5.41046	2.59953	0.27583	H	6.3918	-0.39511	-1.01127
C	6.26161	1.61188	-0.22118	H	3.95677	-0.80751	-0.83564

Table S22. Optimized Z-matrixes of **(2*S**, 3*R**)-c-4** in the gas phase (Å) at the M06-2X/def2-SVP level of theory

C	-4.5912	-0.08352	1.08386	C	5.46212	2.45599	0.49311
C	-3.76379	-1.80024	-1.67244	C	4.09907	2.21661	0.63865
C	-0.79579	-3.61167	-1.30061	O	-0.50414	2.56681	1.90286
C	-2.61955	-1.89702	-0.66569	H	-4.92915	0.3381	2.03842
C	-1.2672	-2.17782	-1.3765	H	-5.19901	0.37618	0.28849
C	-3.12658	0.19079	0.88033	H	-4.79219	-1.16345	1.08233
O	-0.28178	-1.32419	-0.76606	H	-4.73664	-1.68017	-1.17919
C	-1.18686	1.5182	1.33972	H	-3.61116	-0.94207	-2.34354
O	-3.31332	2.14454	2.25713	H	-3.81107	-2.7127	-2.28672
C	-2.30321	-0.63025	0.10245	H	-1.53006	-4.27544	-1.77935
C	-0.93234	-0.39808	-0.02619	H	0.16931	-3.73336	-1.81005
C	-0.34433	0.69697	0.59246	H	-0.67941	-3.91247	-0.24975
C	-2.54736	1.31365	1.50696	H	-2.83383	-2.71519	0.04664
C	2.09268	0.7355	0.08326	H	-1.34972	-1.85882	-2.4312
C	0.829	2.48127	1.55158	H	-2.74876	2.83468	2.62905
C	0.99627	1.26382	0.68521	H	1.85892	-0.17361	-0.48175
O	1.60383	3.29977	1.94055	H	3.87786	-0.6188	-1.23654
C	3.50622	1.10193	0.01545	H	6.30283	-0.18151	-1.48872

C	4.32732	0.24878	-0.74884	H	7.32843	1.79887	-0.3747
C	5.68793	0.49247	-0.89064	H	5.90675	3.32406	0.98194
C	6.26065	1.60117	-0.2675	H	3.48927	2.89024	1.2355

Computational result of 1

Table S23. Experimental and calculated ^{13}C-NMR chemical shifts of **conformers a-c**

No.	$\delta_{exptl.}$	(2*S**, 3*R**)-a-$\delta_{calcd.}$	(2*S**, 3*R**)-b-$\delta_{calcd.}$	(2*S**, 3*R**)-c-$\delta_{calcd.}$
2	88.0	86.0	86.7	87.1
2-CH_3	21.0	21.9	21.8	22.4
3	45.0	46.8	46.8	46.2
3-CH_3	19.4	22.5	21.2	22.1
4	108.6	112.9	107.5	105.4
4-CH_3	11.0	13.1	13.9	15.6
5	146.3	140.6	141.4	118.3
6	112.6	110.6	109.6	125.6
7	135.3	129.9	131.7	159.9
8	142.9	130.6	137.6	141.0
9	133.5	133.9	131.3	129.1
1'	166.7	160.2	160.6	133.8
2'	123.5	119.8	120.5	142.0
3'	142.0	142.2	142.0	122.1
4'	136.6	133.0	133.1	132.7
5'	132.4	131.7	131.4	131.3
6'	129.1	126.3	126.7	126.5
7'	131.1	129.2	129.0	128.9

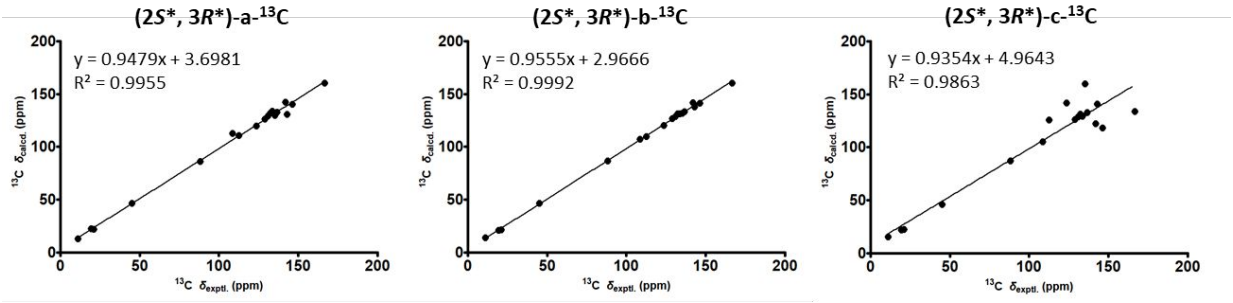


Figure S5. Linear regression between the exptl. and calcd. ^{13}C NMR data of conformers **a-c**

Functional		Solvent?		Basis Set		Type of Data	
mPW1PW91		PCM		6-31+G(d,p)		Unscaled Shifts	
		DP4+	0.00%	100.00%	0.00%	-	-
Nuclei	sp2?	xperimenta	Isomer 1	Isomer 2	Isomer 3	Isomer 4	Isomer 5
C		88.0	86.0	86.7	87.1		
C		21.0	21.9	21.8	22.4		
C		45.0	46.8	46.8	46.2		
C		19.4	22.5	21.2	22.1		
C	x	108.6	112.9	107.5	105.4		
C		11.0	13.1	13.9	15.6		
C	x	146.3	140.6	141.4	118.3		
C	x	112.6	110.6	109.6	125.6		
C	x	135.3	129.9	131.7	159.9		
C	x	142.9	130.6	137.6	141.0		
C	x	133.5	133.9	131.3	129.1		
C	x	166.7	160.2	160.6	133.80		
C	x	123.5	119.8	120.5	142.00		
C	x	142.0	142.2	142.0	122.10		
C	x	136.6	133.0	133.1	132.70		
C	x	132.4	131.7	131.4	131.30		
C	x	129.1	126.3	126.7	126.50		
C	x	131.1	129.2	129.0	128.90		

Figure S6. Detailed DP4+ probability (calculated at mPW1PW91/6-31+G(d,p) level) for **1**. Isomer 1 is **(2*S**, 3*R**)-a**, isomer 2 is **(2*S**, 3*R**)-b**, isomer 2 is **(2*S**, 3*R**)-c**

Table S24. Experimental and calculated ^{13}C-NMR chemical shifts of **(2*S**, 3*R**)-b** and **(2*R**, 3*R**)-b**

No.	$\delta_{exptl.}$	**(2*S**, 3*R**)-b**-$\delta_{calcd.}$	**(2*R**, 3*R**)-b**-$\delta_{calcd.}$
2	88.0	86.7	81.3
2-CH_3	21.0	21.8	17.0
3	45.0	46.8	43.7
3-CH_3	19.4	21.2	16.2
4	108.6	107.5	107.4
4-CH_3	11.0	13.9	14.0
5	146.3	141.4	141.4
6	112.6	109.6	109.5
7	135.3	131.7	131.4
8	142.9	137.6	138.9
9	133.5	131.3	132.4
1'	166.7	160.6	160.5
2'	123.5	120.5	120.2
3'	142.0	142.0	141.6
4'	136.6	133.1	132.8
5'	132.4	131.4	131.5
6'	129.1	126.7	126.7
7'	131.1	129.0	129.0

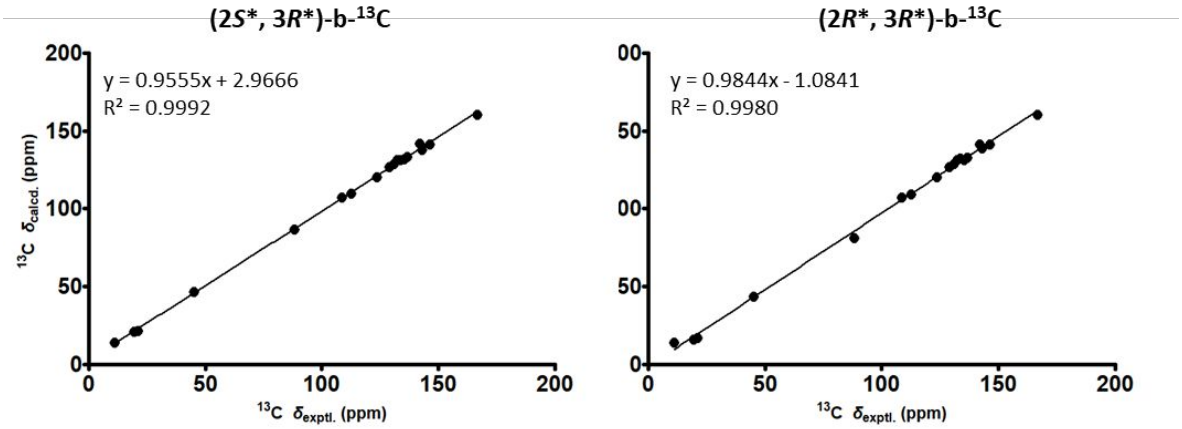


Figure S7. Linear regression between the exptl. and calcd. ^{13}C NMR data of **(2*S**, 3*R**)-b** and **(2*R**, 3*R**)-b**

Table S25. Experimental and calculated ^{1}H-NMR chemical shifts of **(2*S**, 3*R**)-b** and **(2*R**, 3*R**)-b**

No.	$\delta_{exptl.}$	(2*S**, 3*R**)-b-$\delta_{calcd.}$	(2*R**, 3*R**)-b-$\delta_{calcd.}$
2	4.48	4.57	4.89
2-CH_3	1.34	1.34	1.49
3	3.18	3.24	3.37
3-CH_3	1.31	1.33	1.20
4-CH_3	2.18	2.32	2.31
3'	8.23	8.40	8.40
5'	8.13	9.03	9.02
6'	7.46	7.79	7.79
7'	7.45	7.86	7.86

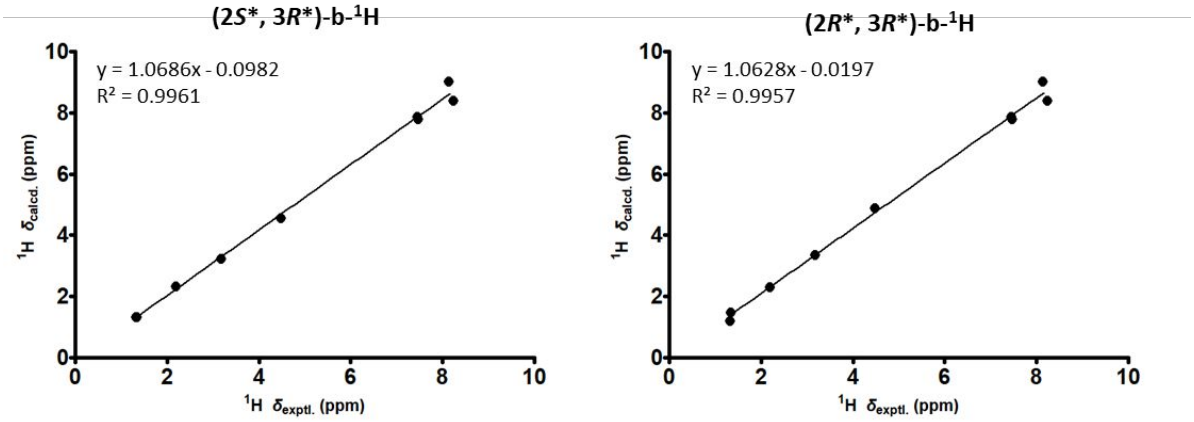


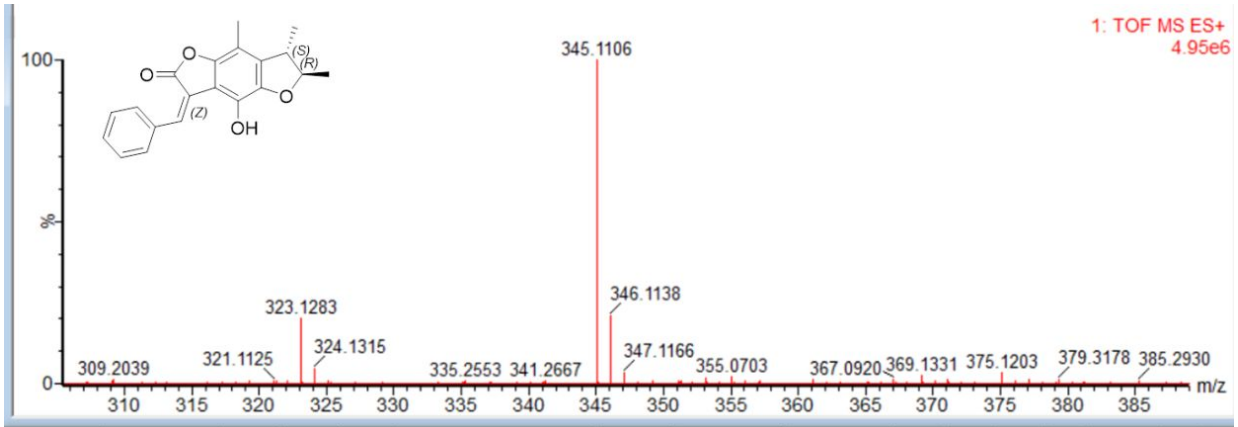
Figure S8. Linear regression between the exptl. and calcd. ^{1}H NMR data of **(2*S**, 3*R**)-b** and **(2*R**, 3*R**)-b**

	A	B	C	D	E	F	G	H
1	Functional		Solvent?		Basis Set		Type of Data	
2	mPW1PW91		PCM		6-31+G(d,p)		Unscaled Shifts	
3								
4			Isomer 1	Isomer 2	Isomer 3	Isomer 4	Isomer 5	Isomer 6
5	sDP4+ (H data)		86.16%	13.84%	-	-	-	-
6	sDP4+ (C data)		99.99%	0.01%	-	-	-	-
7	sDP4+ (all data)		100.00%	0.00%	-	-	-	-
8	uDP4+ (H data)		99.56%	0.44%	-	-	-	-
9	uDP4+ (C data)		100.00%	0.00%	-	-	-	-
10	uDP4+ (all data)		100.00%	0.00%	-	-	-	-
11	DP4+ (H data)		99.93%	0.07%	-	-	-	-
12	DP4+ (C data)		100.00%	0.00%	-	-	-	-
13	DP4+ (all data)		100.00%	0.00%	-	-	-	-

Functional		Solvent?		Basis Set		Type of Data	
mPW1PW91		PCM		6-31+G(d,p)		Unscaled Shifts	
		DP4+	100.00%	0.00%	-	-	-
Nuclei	sp2?	xperimenta	Isomer 1	Isomer 2	Isomer 3	Isomer 4	Isomer 5
C		11.0	13.9	14.0			
C		19.4	21.2	16.2			
C		21.0	21.8	17.0			
C		45.0	46.8	43.7			
C		88.0	86.7	81.3			
C	x	142.0	142.0	141.6			
C	x	166.7	160.6	160.5			
C	x	112.6	109.6	109.5			
C	x	123.5	120.5	120.2			
C	x	108.6	107.5	107.4			
C	x	133.5	131.3	132.4			
C	x	142.9	137.6	138.9			
C	x	135.3	131.7	131.4			
C	x	146.3	141.4	141.4			
C	x	136.6	133.1	132.8			
C	x	132.4	131.4	131.5			
C	x	129.1	126.7	126.7			
C	x	131.1	129.0	129.0			
H		1.31	1.33	1.2			
H		1.34	1.34	1.49			
H		2.18	2.32	2.31			
H		3.18	3.24	3.37			
H		4.48	4.57	4.89			
H	x	7.45	7.86	7.86			
H	x	7.46	7.79	7.79			
H	x	8.13	9.03	9.02			
H	x	8.23	8.4	8.4			

Figure S9. Detailed DP4+ probability (calculated at mPW1PW91/6-31+G(d,p) level) for **1**. Isomer 1 is **(2*S**, 3*R**)-b**, isomer 2 is **(2*R**, 3*R**)-b**

Original spectroscopic data of 1



Mass	Calc. Mass	mDa	PPM	DBE	Formula	i-FIT	i-FIT Norm	Fit Conf %	C	H	N	O	Na	Cl	Br
345.1106	345.1103	0.3	0.9	11.5	C20 H18 O4 Na	1344.6	0.066	93.57	20	18		4	1		
	345.1087	1.9	5.5	10.5	C17 H17 N2 O6	1348.0	3.486	3.06	17	17	2	6			
	345.1100	0.6	1.7	15.5	C18 H13 N6 O2	1348.6	4.094	1.67	18	13	6	2			
	345.1127	-2.1	-6.1	14.5	C22 H17 O4	1349.3	4.700	0.91	22	17		4			
	345.1116	-1.0	-2.9	16.5	C21 H14 N4 Na	1349.7	5.197	0.55	21	14	4		1		
	345.1140	-3.4	-9.9	19.5	C23 H13 N4	1351.5	6.974	0.09	23	13	4				

Figure S10. HRESIMS spectrum of **1**

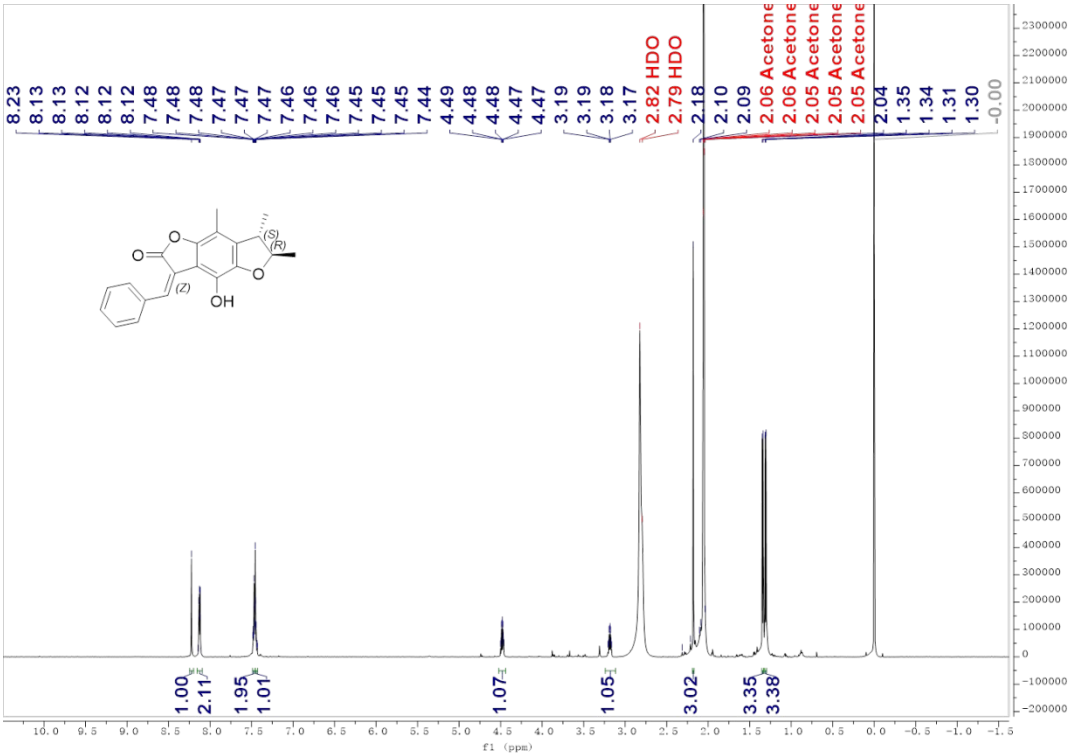


Figure S11. ^{1}H NMR spectrum of **1** in acetone-*d*

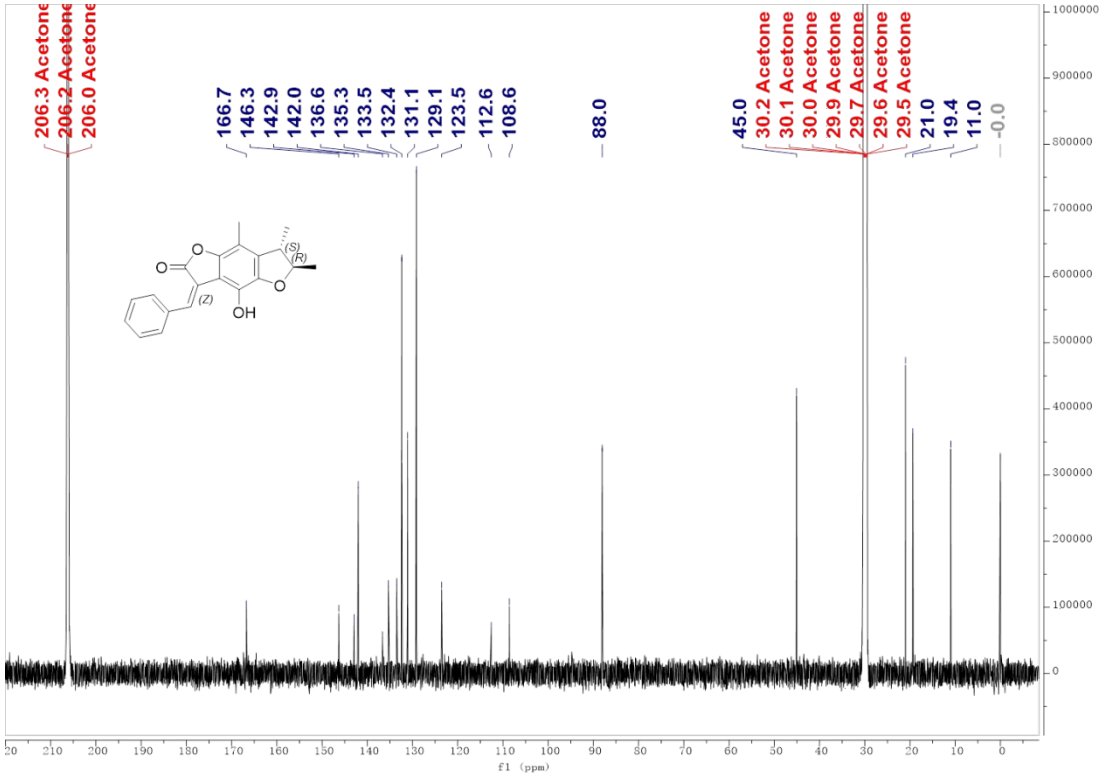


Figure S12. ^{13}C NMR spectrum of **1** in acetone-*d*

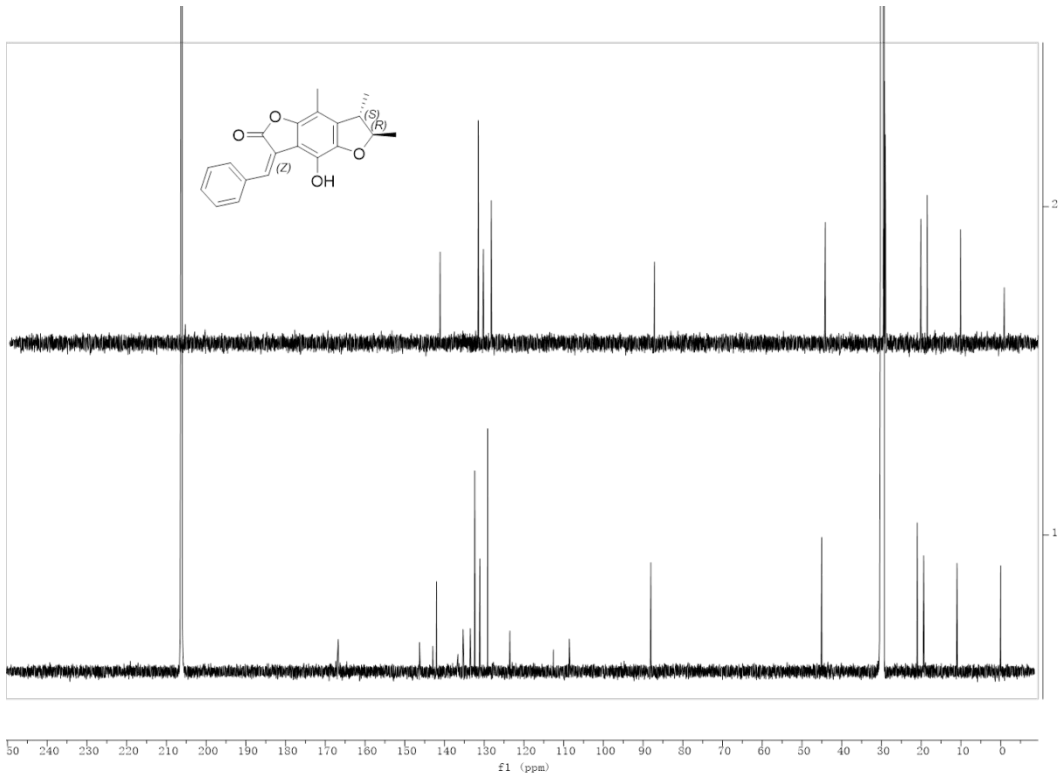


Figure S13. ^{13}C/DEPT spectrum of **1** in acetone-*d*

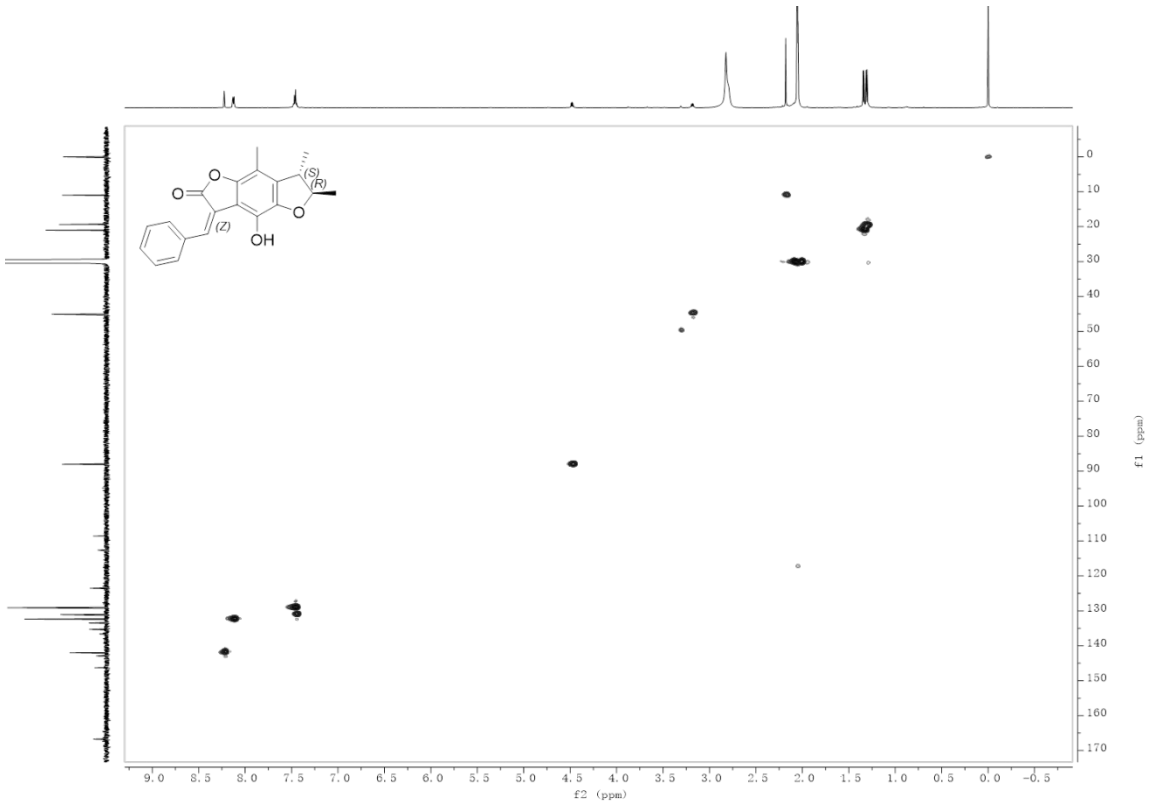


Figure S14. HSQC spectrum of **1** in acetone-*d*

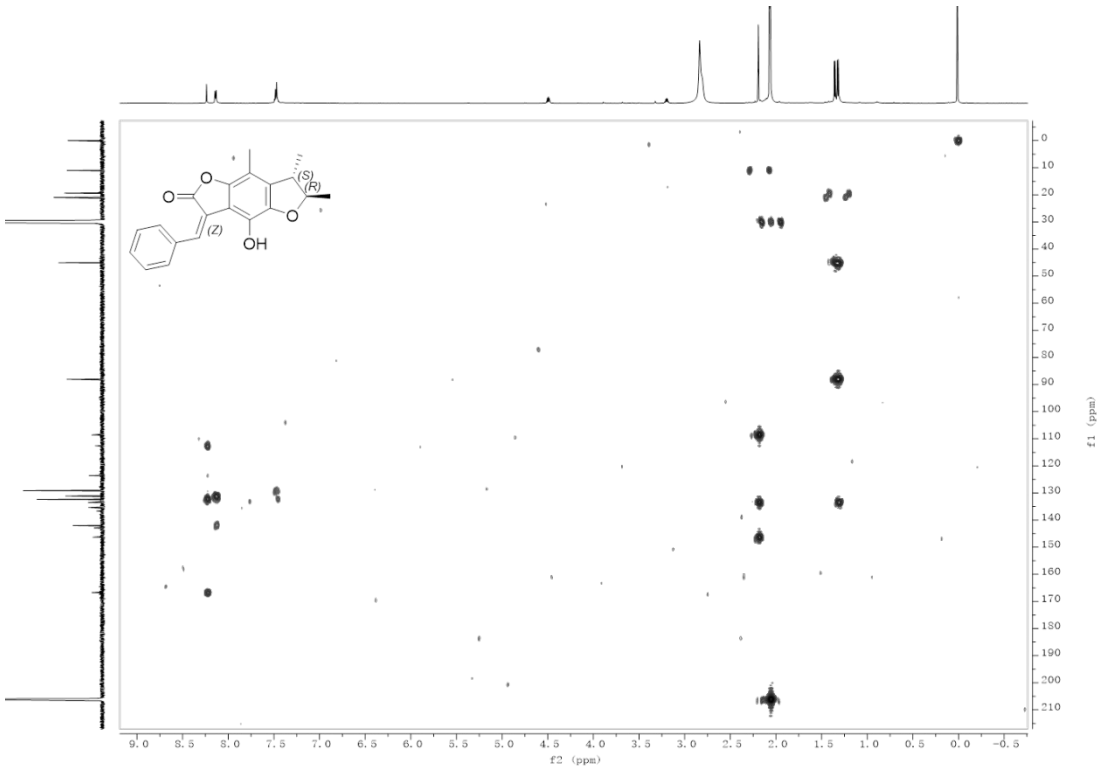


Figure S15. HMBC spectrum of **1** in acetone-*d*

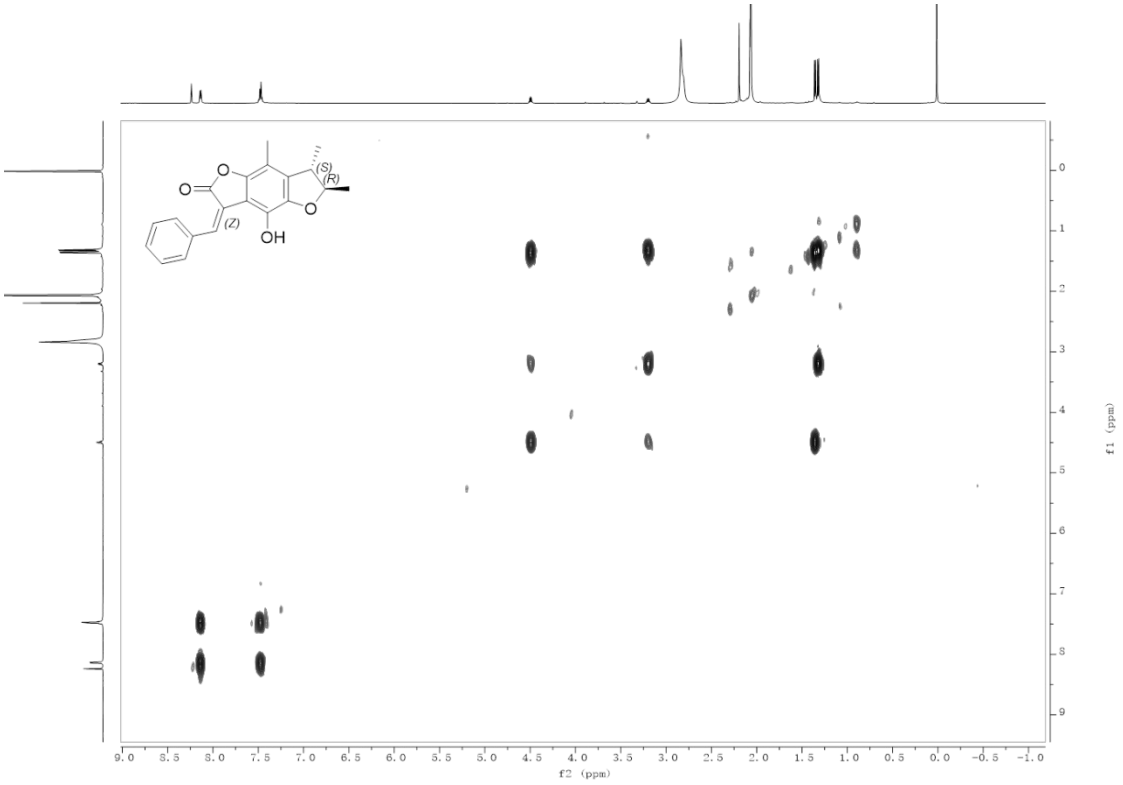


Figure S16. COSY spectrum of **1** in acetone-*d*

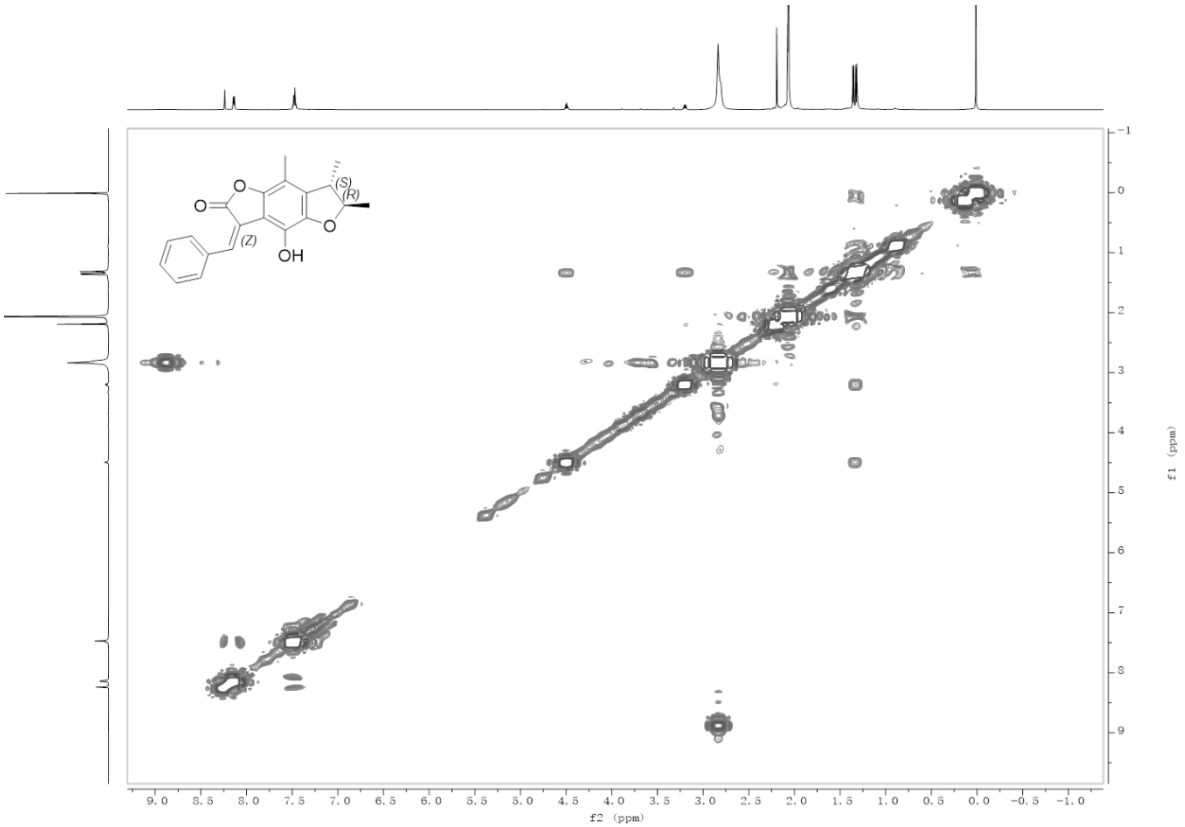


Figure S17. NOESY spectrum of **1** in acetone-*d*

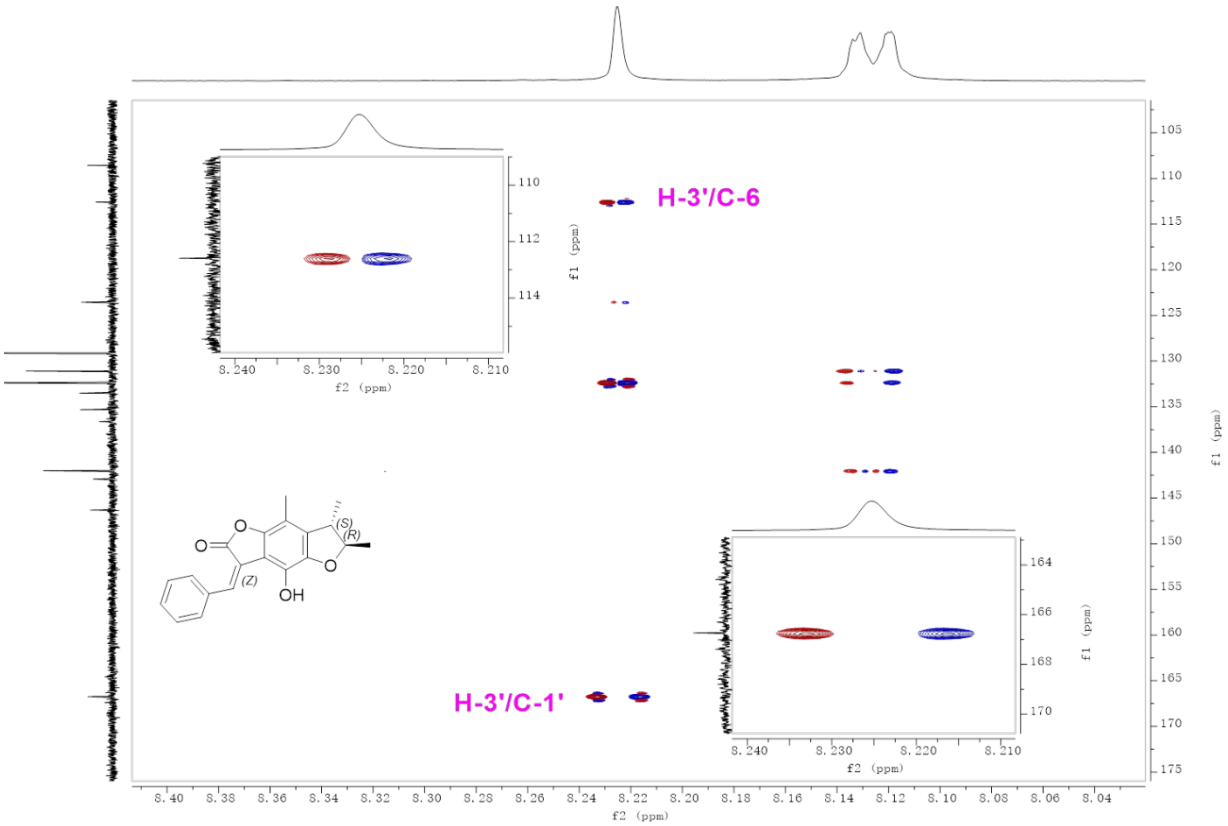


Figure S18. HSQMBC spectrum of **1** in acetone-*d*

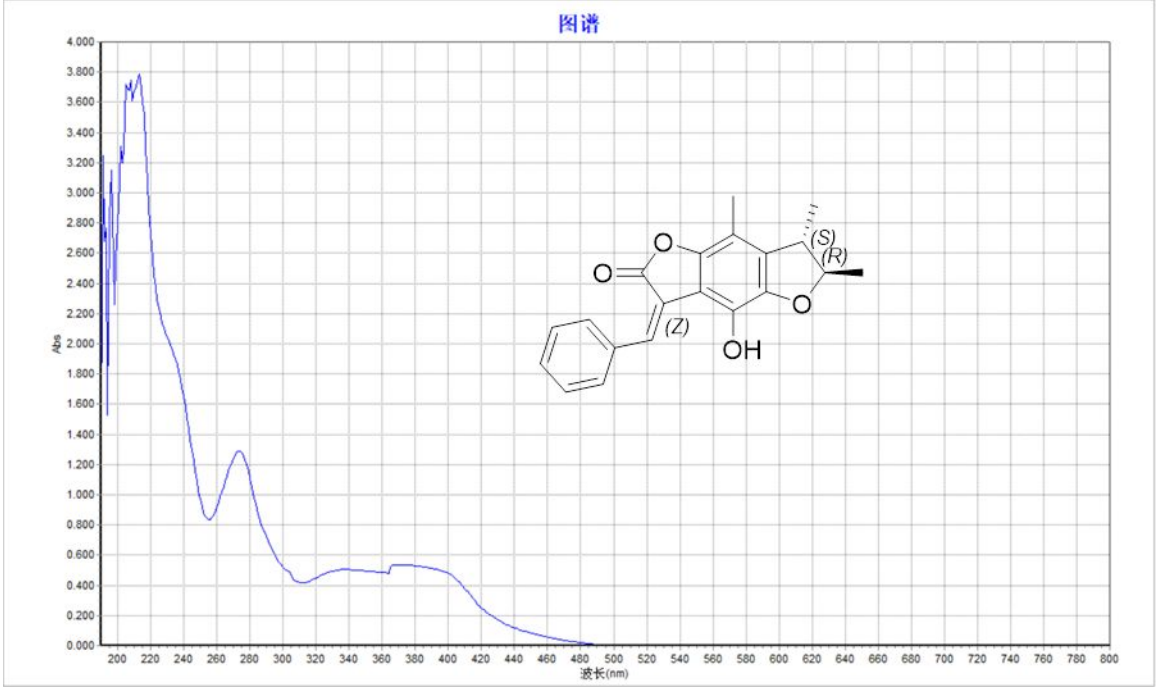


Figure S19. UV spectrum of **1**

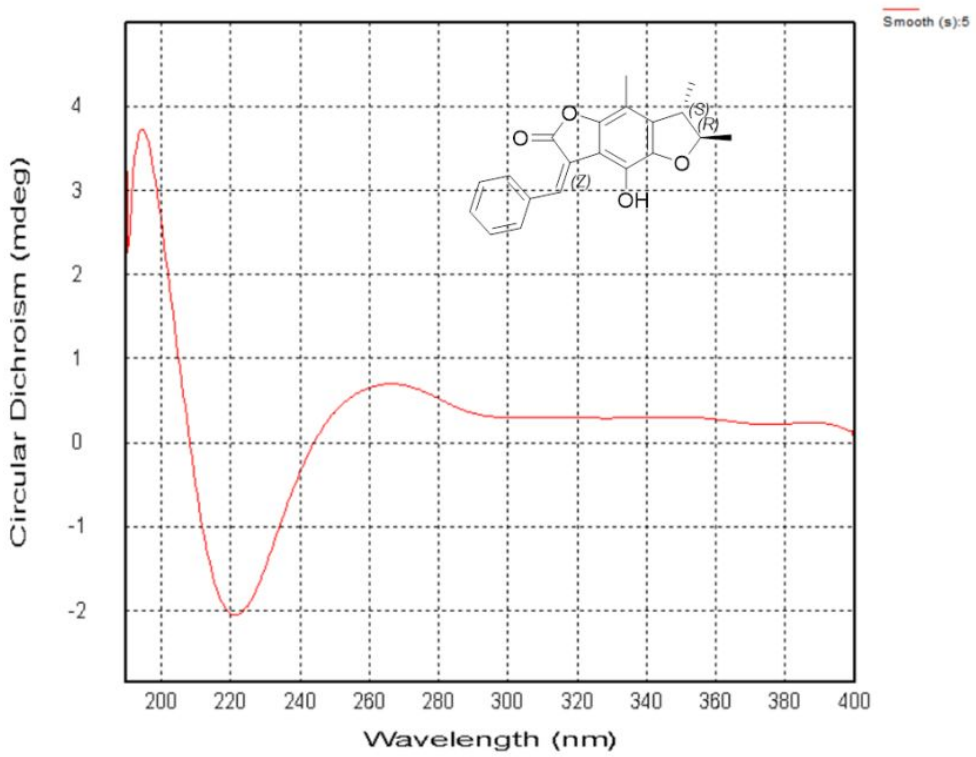


Figure S20. ECD spectrum of **1**

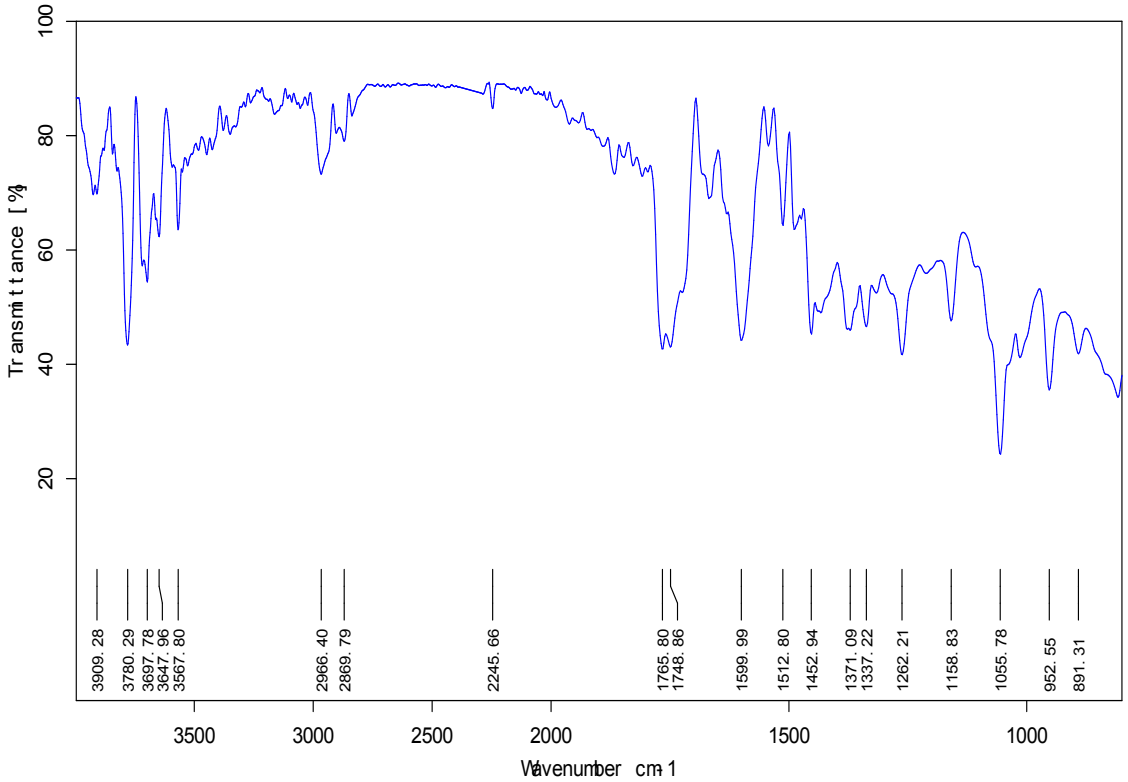


Figure S21. IR spectrum of **1**

Table S26. Key transitions, oscillator strengths, and rotatory strengths in the ECD spectrum of conformer **(2*S*, 3*R*)-b-1** at the CAM-B3LYP-SCRF/def2-SVP//M06-2X-D3/def2-SVP level of theory in MeOH with IEFPCM solvent model.

Num	transition	CI-coeff	ΔE (eV)	λ (nm)	f	Rvel	Rlen
1	85->86	0.67101	3.5094	353.29	0.3811	-0.8941	-1.5091
2	84->86	0.67512	3.6499	339.70	0.4999	5.6714	5.4848
3	83->86	0.63489	4.6932	264.18	0.0148	-1.7553	-2.3472
4	81->86	0.64132	4.8086	257.84	0.0002	1.8241	2.2351
5	82->86	0.59673	5.0406	245.97	0.2284	9.0581	9.4041
	85->88	0.27309					
6	82->86	-0.28823	5.2921	234.28	0.0738	-9.3605	-7.5112
	84->90	-0.23078					
	85->88	0.55414					
7	84->88	0.4932	5.7745	214.71	0.0091	-7.3645	-5.6641
	85->90	0.38296					
8	83->86	0.27757	5.8566	211.70	0.1473	22.5366	20.0789
	84->87	0.47267					
	85->87	0.29368					
9	80->86	0.54439	6.1593	201.30	0.0530	-13.7421	-15.2926
	84->88	-0.26648					
10	80->86	0.22425	6.2594	198.08	0.1561	7.4618	7.6656
	83->87	0.24688					
	84->89	0.32904					
	84->90	0.27277					
	85->89	0.38201					
11	84->88	-0.29058	6.3217	196.13	0.6932	59.5	54.5141
	84->89	0.31094					
	85->90	0.31743					
12	84->88	-0.23067	6.4583	191.98	0.4399	-4.702	-7.1547
	84->90	0.45293					
	85->88	0.22569					
	85->90	0.31335					
13	76->86	-0.41353	6.5371	189.66	0.0012	-0.4268	-0.1294
	77->86	0.51162					
14	84->91	-0.267	6.6448	186.59	0.0240	-60.8428	-49.1083
	85->87	0.33117					
	85->91	0.36077					
15	84->87	-0.28163	6.6698	185.89	0.0215	-29.6025	-29.6645
	85->87	0.50825					
	85->91	-0.23198					
16	78->86	0.39311	6.7162	184.60	0.0921	29.3342	26.9357
	83->87	0.35714					
17	73->86	0.25166	6.8308	181.51	0.0028	-15.0556	-15.7938
	74->86	0.41952					
	76->86	0.24567					
18	84->89	-0.38692	6.9033	179.60	0.0478	-0.238	-0.5306
	85->89	0.42069					
19	82->87	-0.32325	7.0291	176.39	0.0308	-1.7056	-1.241
	83->89	0.42207					
	84->87	0.32088					
20	78->86	0.43797	7.1005	174.61	0.2359	2.8036	2.6843

	83->87	-0.41473					
21	84->91	0.38907	7.1929	172.37	0.0019	8.9587	5.153
	84->92	-0.30346					
	85->91	0.42818					
22	73->86	0.44488	7.3043	169.74	0.0062	2.1503	2.2708
	79->86	0.3058					
23	79->86	0.49726	7.4836	165.67	0.0103	1.4071	2.4827
24	85->91	0.2373	7.5098	165.10	0.0029	8.0731	6.8238
	85->92	0.57401					
25	80->88	-0.25105	7.6195	162.72	0.0783	14.6909	14.819
	82->88	0.58973					
26	81->88	0.27171	7.6633	161.79	0.0043	-3.4453	-4.4158
	81->89	0.23207					
27	82->87	0.45915	7.6988	161.04	0.3750	2.3517	3.0321
	83->89	0.44965					
28	76->87	-0.29148	7.8057	158.84	0.0043	-9.0278	-9.7397
	77->87	0.26631					
	81->87	0.36778					
29	69->86	0.30089	7.8278	158.39	0.0043	-10.8743	-10.8055
	77->86	0.2609					
30	84->91	0.2791	7.8577	157.79	0.0106	-8.1244	-6.1354
	84->92	0.47582					

Number of the excited states; Only transitions with contribution over 10.0% were listed; Configuration-interaction coefficient; Excitation energy; Wavelength; Oscillator strength; Rotatory strength in velocity form (10^{-40} cgs); Rotatory strength in length form (10^{-40} cgs).

Table S27. Key transitions, oscillator strengths, and rotatory strengths in the ECD spectrum of conformer **(2*S*, 3*R*)-b-2** at the CAM-B3LYP-SCRF/def2-SVP//M06-2X-D3/def2-SVP level of theory in MeOH with IEFPCM solvent model.

Num	transition	CI-coeff	ΔE (eV)	λ (nm)	f	Rvel	Rlen
1	85->86	0.67096	3.5110	353.13	0.3894	-1.6454	-2.2811
2	84->86	0.67495	3.6512	339.57	0.4930	5.4294	5.2626
3	83->86	0.63516	4.6935	264.16	0.0148	-1.4158	-1.9062
4	81->86	0.64094	4.8095	257.79	0.0002	1.3344	1.6849
5	82->86	0.59777	5.0426	245.87	0.2273	9.0283	9.3906
	85->88	0.26919					
6	82->86	-0.28631	5.2930	234.24	0.0742	-9.323	-7.4585
	84->90	-0.23168					
	85->88	0.55484					
7	84->88	0.4948	5.7752	214.68	0.0087	-7.1326	-5.4137
	85->90	0.37952					
8	83->86	0.2772	5.8573	211.68	0.1474	22.859	20.3076
	84->87	0.46942					
	85->87	0.2968					
9	80->86	0.54729	6.1590	201.30	0.0503	-13.8745	-15.3789
	84->88	-0.26038					
10	83->87	0.24988	6.2598	198.06	0.1475	7.3224	7.5354
	84->89	0.33523					
	84->90	0.26578					
	85->89	0.38535					
11	84->88	-0.29353	6.3218	196.12	0.6972	61.4266	56.3094

	84->89	0.29924					
	85->90	0.32483					
12	84->88	-0.22728	6.4616	191.88	0.4483	-2.2945	-4.0521
	84->90	0.45643					
	85->88	0.22732					
	85->90	0.31238					
13	76->86	-0.41371	6.5383	189.63	0.0012	-0.2179	0.0161
	77->86	0.51192					
14	84->91	-0.26774	6.6486	186.48	0.0290	-65.7649	-54.1218
	85->87	0.32196					
	85->91	0.35553					
15	84->87	-0.28868	6.6734	185.79	0.0226	-29.8958	-29.8976
	85->87	0.51148					
16	78->86	0.3878	6.7185	184.54	0.0884	31.3649	28.9573
	83->87	0.35289					
17	73->86	0.25487	6.8306	181.51	0.0026	-14.5412	-15.2416
	74->86	0.4173					
	76->86	0.24638					
18	84->89	-0.39062	6.9056	179.54	0.0461	-0.0961	-0.5215
	85->89	0.41994					
19	82->87	-0.32296	7.0290	176.39	0.0312	-1.7992	-1.3735
	83->89	0.42201					
	84->87	0.32038					
20	78->86	0.43839	7.1003	174.62	0.2372	3.0455	3.0241
	83->87	-0.41413					
21	84->91	0.38268	7.1919	172.40	0.0021	8.8944	5.0104
	84->92	-0.30579					
	85->91	0.43195					
22	73->86	0.44649	7.3036	169.76	0.0063	2.1187	2.2388
	79->86	0.30711					
23	79->86	0.49549	7.4814	165.72	0.0109	2.2039	3.3081
24	85->91	0.24026	7.5091	165.11	0.0028	8.1264	6.8304
	85->92	0.57242					
25	80->88	-0.25054	7.6174	162.77	0.0771	14.7811	15.0582
	82->88	0.58797					
26	81->88	0.27057	7.6634	161.79	0.0041	-3.6755	-4.6277
	81->89	0.23801					
27	82->87	0.45939	7.6992	161.04	0.3746	3.1022	3.585
	83->89	0.44999					
28	76->87	-0.28914	7.8059	158.83	0.0043	-9.6227	-10.2953
	77->87	0.26437					
	81->87	0.36319					
29	69->86	0.29224	7.8260	158.43	0.0041	-10.0434	-9.976
	77->86	0.25518					
30	84->91	0.28613	7.8540	157.86	0.0106	-8.3498	-6.2245
	84->92	0.47541					

Number of the excited states; Only transitions with contribution over 10.0% were listed; Configuration-interaction coefficient; Excitation energy; Wavelength; Oscillator strength; Rotatory strength in velocity form (10^{-40} cgs); Rotatory strength in length form (10^{-40} cgs).

Table S28. Key transitions, oscillator strengths, and rotatory strengths in the ECD spectrum of conformer **(2*S*, 3*R*)-b-3** at the CAM-B3LYP-SCRF/def2-SVP//M06-2X-D3/def2-SVP level of theory in MeOH with IEFPCM solvent model.

Num	transition	CI-coeff	ΔE (eV)	λ (nm)	f	Rvel	Rlen
1	85->86	0.67506	3.5066	353.58	0.4052	-3.2918	-2.72
2	84->86	0.67871	3.6512	339.57	0.4860	-1.707	-1.1447
3	83->86	0.63571	4.6926	264.21	0.0148	0.0681	0.1774
4	80->86	-0.29366	4.8106	257.73	0.0003	-0.1038	-0.3039
	81->86	0.58518					
5	82->86	0.59532	5.0386	246.07	0.2281	0.4496	0.3076
	85->88	0.26315					
6	82->86	-0.29023	5.2754	235.02	0.0719	0.8219	-0.3839
	84->90	-0.22888					
	85->88	0.55252					
7	84->88	0.50073	5.7594	215.27	0.0091	3.6576	2.5605
	85->90	0.37102					
8	83->86	0.27868	5.8563	211.71	0.1423	-10.2185	-8.5573
	84->87	0.45948					
	85->87	0.31693					
9	80->86	0.51405	6.1341	202.12	0.0444	-1.5098	-1.5325
	81->86	0.25382					
	84->88	-0.24923					
10	83->87	0.23694	6.2559	198.19	0.1858	-2.3781	-2.5616
	84->89	0.33108					
	84->90	0.25492					
	85->89	0.4172					
11	84->88	-0.30683	6.3108	196.46	0.6448	-32.3068	-29.9986
	84->89	0.28605					
	85->90	0.37252					
12	84->90	0.48365	6.4621	191.86	0.5153	20.4467	23.9125
	85->88	0.23537					
	85->90	0.28245					
13	76->86	0.31696	6.5361	189.69	0.0008	-0.2075	-0.3437
	77->86	0.54791					
14	84->87	-0.34086	6.6728	185.81	0.0029	2.9491	0.5937
	85->87	0.57202					
15	84->91	-0.31951	6.6936	185.23	0.0127	47.1229	39.6536
	84->92	0.2554					
	85->91	0.36995					
	85->92	-0.25741					
16	78->86	0.38609	6.7125	184.71	0.1043	-21.4134	-18.479
	83->87	0.37155					
17	74->86	0.45709	6.8266	181.62	0.0003	3.9542	4.3651
	75->86	-0.22465					
18	84->89	-0.40408	6.9113	179.39	0.0389	1.8225	0.9053
	85->89	0.40997					
19	82->87	-0.32047	7.0286	176.40	0.0322	-0.2242	0.0887
	83->89	0.4186					
	84->87	0.32018					
20	78->86	0.42063	7.0965	174.71	0.2452	0.5175	1.3205
	83->87	-0.41268					

21	84->91	0.35636	7.2302	171.48	0.0027	-7.0476	-6.1593
	84->92	-0.31782					
	85->91	0.40195					
22	73->86	0.36362	7.2848	170.19	0.0040	-6.3908	-6.3603
	74->86	-0.2432					
	79->86	0.37523					
23	73->86	-0.22723	7.4526	166.36	0.0071	6.8584	4.9803
	79->86	0.45352					
24	85->91	0.30829	7.5073	165.15	0.0057	5.88	3.3071
	85->92	0.53243					
25	82->88	0.55521	7.5810	163.55	0.0618	-7.5458	-4.1567
26	81->88	0.23765	7.6594	161.87	0.0035	11.823	11.6188
	81->89	0.22818					
27	82->87	0.45898	7.6981	161.06	0.3756	-0.8771	-1.7817
	83->89	0.45022					
28	77->87	0.29753	7.8027	158.90	0.0154	10.8627	12.6949
	81->87	0.35075					
29	69->86	-0.2461	7.8245	158.46	0.0454	30.1832	29.1408
	76->86	0.32989					
	77->86	-0.22898					
30	84->91	0.30653	7.9082	156.78	0.0281	-13.3534	-11.2734
	84->92	0.44376					

Number of the excited states; Only transitions with contribution over 10.0% were listed; Configuration-interaction coefficient; Excitation energy; Wavelength; Oscillator strength; Rotatory strength in velocity form (10^{-40} cgs); Rotatory strength in length form (10^{-40} cgs).

Table S29. Key transitions, oscillator strengths, and rotatory strengths in the ECD spectrum of conformer **(2*S*, 3*R*)-b-4** at the CAM-B3LYP-SCRF/def2-SVP//M06-2X-D3/def2-SVP level of theory in MeOH with IEFPCM solvent model.

Num	transition	CI-coeff	ΔE (eV)	λ (nm)	f	Rvel	Rlen
1	85->86	0.67499	3.5076	353.48	0.4128	-2.3705	-1.9409
2	84->86	0.67846	3.6520	339.50	0.4788	-7.3736	-6.8779
3	83->86	0.63523	4.6934	264.17	0.0148	0.8663	1.2095
4	80->86	-0.3023	4.8119	257.66	0.0003	-1.0718	-1.5125
	81->86	0.58072					
5	82->86	0.59617	5.0388	246.06	0.2279	-0.6238	-0.6076
	85->88	0.26022					
6	82->86	-0.28897	5.2753	235.03	0.0723	4.5147	3.1243
	84->90	-0.22917					
	85->88	0.55217					
7	84->88	0.50102	5.7580	215.33	0.0092	3.8506	2.8499
	85->90	0.36895					
8	83->86	0.27904	5.8562	211.71	0.1424	-8.8633	-6.8194
	84->87	0.45679					
	85->87	0.32049					
9	80->86	0.50961	6.1324	202.18	0.0438	-0.9694	-1.0433
	81->86	0.264					
	84->88	-0.24754					
10	83->87	0.23714	6.2553	198.21	0.1833	-4.1813	-4.1924
	84->89	0.33111					
	84->90	0.25174					

	85->89	0.42023					
11	84->88	-0.30655	6.3093	196.51	0.6394	-38.8782	-35.5786
	84->89	0.28281					
	85->90	0.3762					
12	84->90	0.48491	6.4623	191.86	0.5220	19.1207	22.2514
	85->88	0.23537					
	85->90	0.28098					
13	76->86	0.34235	6.5373	189.66	0.0007	1.1586	0.997
	77->86	0.54034					
14	84->87	-0.33758	6.6735	185.79	0.0030	4.8994	1.4863
	85->87	0.55799					
15	84->91	-0.30053	6.6968	185.14	0.0227	58.0281	49.7996
	84->92	0.24406					
	85->91	0.33836					
	85->92	-0.24053					
16	78->86	0.36711	6.7135	184.68	0.0955	-33.9757	-30.2195
	83->87	0.35316					
17	74->86	0.45319	6.8269	181.61	0.0022	12.993	13.7469
	75->86	-0.22773					
18	84->89	-0.40719	6.9129	179.35	0.0387	2.3716	1.5407
	85->89	0.40696					
19	82->87	-0.32108	7.0282	176.41	0.0318	-0.0989	0.2465
	83->89	0.41785					
	84->87	0.31947					
20	78->86	0.42367	7.0965	174.71	0.2453	0.5901	1.3626
	83->87	-0.41127					
21	84->91	0.35106	7.2305	171.47	0.0029	-7.534	-6.4294
	84->92	-0.31697					
	85->91	0.40299					
22	73->86	0.36422	7.2850	170.19	0.0043	-6.6447	-6.6318
	74->86	-0.24325					
	79->86	0.37523					
23	73->86	-0.22781	7.4497	166.43	0.0077	6.6135	4.6261
	79->86	0.45349					
24	85->91	0.31124	7.5065	165.17	0.0065	5.3406	2.8034
	85->92	0.52856					
25	82->88	0.55225	7.5785	163.60	0.0601	-8.2821	-4.7771
26	81->88	0.23795	7.6595	161.87	0.0027	10.3839	10.3434
	81->89	0.22961					
27	82->87	0.45824	7.6977	161.07	0.3767	3.0592	1.9803
	83->89	0.45062					
28	76->86	0.25233	7.8037	158.88	0.0235	16.4447	18.4565
	77->87	0.27284					
	81->87	0.3207					
29	69->86	-0.24811	7.8184	158.58	0.0372	22.4703	21.2514
	76->86	0.28414					
30	84->91	0.31319	7.9067	156.81	0.0282	-9.4519	-7.321
	84->92	0.44276					

Number of the excited states; Only transitions with contribution over 10.0% were listed; Configuration-interaction coefficient; Excitation energy; Wavelength; Oscillator strength; Rotatory strength in velocity form (10^{-40} cgs); Rotatory strength in length form (10^{-40} cgs).