Electronic Supplementary Material (ESI) for Organic & Biomolecular Chemistry.

Supplementary Data

Sarocladione, a unique 5,10:8,9-di*seco*-steroid from the deep-sea-derived fungus *Sarocladium kiliense*

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Detailed experimental procedures

General Experimental Procedures. Optical rotations were measured with an Anton Paar MCP 500 polarimeter. NMR spectra were recorded on a Bruker Avance II 400 MHz spectrometer with TMS as an internal standard. HRESIMS were completed on a Waters Xevo G2 Q-TOF spectrometer. Materials for column chromatography were silica gel (Qingdao Marine Chemistry Co. Ltd., Qingdao, China), Sephadex LH-20 (Amersham Pharmacia Biotech AB, Uppsala, Sweden), and ODS (50 μm, Daiso, Japan).

Fungus Material. *Sarocladium killiense* was isolated from a deep-sea sediment sample of the Northeast Pacific Ocean (−5070 m). It was provided by the Marine Culture Collection of China (MCCC). And the voucher specimen of this strain was preserved there with the accession number of 3A00626.

Cultivation and Extraction. *Sarocladium killiense* was cultured on a PDA plate at 28 °C for 5 d. The fresh mycelia and spores were inoculated to 500 mL Erlenmeyer flasks (×16) containing 125 mL A5 medium (4 g D-glucose, 10 g malt extract, 4 g yeast extract, 30 g marine salt, and 1 L water), and was cultured in a rotary shaker with 160 rpm at 28 °C for 4 days. Then the spore cultures were used to inoculate 100 × 1 L Erlenmeyer flasks containing 100 g of oats and 120 mL of distilled water to perform the large-scale fermentation. After 30 days, the fermented broth was extracted with EtOAc for five times. The organic solvent was evaporated and defatted by partitioning with petroleum ether (PE) to afford a crude extract.

Isolation and Purification. The crude extract (106.5 g) was subjected to medium pressure liquid chromatography (MPLC) over silica gel eluting with gradient CH_2Cl_2-MeOH to give six fractions (Fr.1 – Fr.6). Fraction Fr.1 (10.3 g) was further MPLC over ODS (MeOH-H_2O, 50:50→100:0) and column chromatography (CC) over Sephadex LH – 20 (CH_2Cl_2-MeOH, 1:1). Further purification by preparative TLC (PE-EtOAc, 20:1 and 10:1) afforded **1** (8.5 mg), **5** (186.9 mg), and **10** (12.6 mg). Fraction Fr.2 (8.0 g) was subjected to MPLC over ODS (MeOH-H_2O, 80:20→100:0) and CC over Sephadex LH–20 (MeOH). Further purification by CC over silica gel (PE-EtOAc, 30:1) gave **6** (17.2 mg) and by preparative TLC (PE-EtOAc, 10:1) provided **7** (8.2 mg). Fraction Fr.3 (13.0 g) was divided into 14 subfractions (Fr.3.1 –

Fr.3.14) by CC over ODS (MeOH-H_2O, 5:95→100:0) and Sephadex LH－20 (CH_2Cl_2-MeOH, 1:1). Compounds **3** (14.8 mg), **4** (9.7 mg), **18** (21.1 mg), and **19** (20.7 mg) were obtained from Fr.3.1 (269.5 mg), Fr.3.6 (1028.3 mg) and Fr.3.7 (42.3 mg) after purification by CC over silica gel (PE-EtOAc, 3:1; 2:1; 20:1 and PE-acetone, 10:1). Compounds **2** (59.6 mg), **8** (8.4 mg), **11** (4.8 mg), **15** (5.2 mg), **16** (36.7 mg), **17** (16.0 mg), and **20** (31.9 mg) were obtained from Fr.3.2 (102.7 mg), Fr.3.3 (122.6 mg), Fr.3.4 (68.4 mg), Fr.3.5 (80.8 mg), and Fr.3.11 (336.6 mg) by preparative TLC using PE-EtOAc (1:1; 10:1; 20:1; 30:1) or dichloromethane-acetone (5:1; 20:1). Compounds **9** (15.0 mg), **12** (14.0 mg), **13** (28.6), and **14** (160.5 mg) were obtained from fraction Fr.4 (3.1 g) and Fr.5 (3.7 g), respectively, after MPLC over ODS (MeOH-H_2O, 5:95→100:0), followed by CC over Sephadex LH-20 (CH_2Cl_2-MeOH, 1:1). Fraction Fr.6 (5.8 g) was subjected to MPLC over ODS (MeOH-H_2O, 50:50→100:0). Further purification by CC over sephadex LH－20 (CH_2Cl_2-MeOH, 1:1) and by preparative TLC (CH_2Cl_2-MeOH, 10:1) provided **21** (5.0 mg)

Cytotoxic Bioassay. The experiment was conducted using MTT method. Briefly, five human cancer cell lines of SHG-44, 7402, ECA-109, Hela-S3, and PANC-1 were seeded to 96-well plates to incubate for 24 h. Then the tested compounds and *cis*-DDP were added to each well, and the incubation was continued for 48 h. Subsequently, MTT was added and incubated for another 4 h. The liquid supernatant was removed softly and DMSO was added. The absorbencies were measured at 490 nm.

Computational methods

Conformational Analysis. Conformational analysis was initially performed using RDKit Toolkit by Genetic algorithm (GA) at MMFF94 force field for the four configurations **a**–**d** of **1**. RMSD cutoff was set as 0.5 Å and energy window as 7 kcal/mol. Energies of dominating conformers (Boltzmann population > 1%) were provided in Table S1.

NMR Calculation. Conformers were delivered to geometry optimization and NMR calculation by Gaussian 09. First, all conformers were optimized at PM6 using semi-empirical theory method, and then optimized at B3LYP/6-311+G(d,p) in gas phase (Tables S2 and S3). Room-temperature equilibrium populations were calculated

according to the Boltzmann distribution law of $\frac{N_i}{N} = \frac{g_i e^{-\frac{E_i}{k_B T}}}{\sum g_i e^{-\frac{E_i}{k_B T}}}$, where N_i is the number of conformer i with energy E_i and degeneracy g_i at temperature T, and k_B is Boltzmann constant. The conformers with Boltzmann-based distribution higher than 5% were chosen for NMR calculations. The theoretical calculation of NMR was conducted using the Gauge-Including Atomic Orbitals (GIAO) method at mPW1PW91/6-311+G(2d,p) in methanol by the IEFPCM model. Finally, the TMS-corrected NMR chemical shift values were averaged according to Boltzmann distribution and fitted to the experimental values by linear regression. The calculated ^{13}C- and ^{1}H-NMR chemical shift values of TMS in Chloroform were 187.18 ppm and 31.73 ppm, respectively.

Energies and coordinates

Energies at MMFF94 Force Field. Systematic conformational search was performed by RDKit Toolkit at MMFF94 force field. Conformers were filtered by RMSD threshold of 0.5 Å and energy window of 7 kcal/mol, and only those with Boltzmann-based population over 1% were selected for further calculations.

Energies at B3LYP Theory Level. Structures for NMR calculations were optimized at B3LYP/6-311+G(d,p) in gas phase and only conformers with high Boltzmann-based population (> 5%) were retained.

Experimental and computed NMR chemical shifts

^{13}C- and ^{1}H-NMR Chemical Shifts. Computed ^{13}C- and ^{1}H-NMR chemical shifts of each conformer were first Boltzmann-weighted averaged, and then fitted to experimental values by Ordinary Least Squares (OLS) linear regression method in order to remove systematic error that results from the conformational search and random error from experimental conditions.

All computed ^{13}C-NMR chemical shifts showed comparably high correlations to the experimental values (Table S4)

Table S, while configuration **c** had the highest R^2 value and least CMAD and CLAD in ^{1}H-NMR chemical shifts (Table 2).

Table S1 Energies of compound **1** at MMFF94 force field.

Configuration	conformer	Energy (kcal/mol)	Population (%)
a	1	83.93	37.61
a	2	84.45	15.47
a	3	84.63	11.43
a	4	84.74	9.52
a	5	84.93	6.92
a	6	85.40	3.14
a	7	85.41	3.09
a	8	85.62	2.15
a	9	85.92	1.31
a	10	85.95	1.23
a	11	86.04	1.06
b	1	83.37	36.85
b	2	83.40	35.06
b	3	84.13	10.25
b	4	84.66	4.20
b	5	84.71	3.87
b	6	85.17	1.76
c	1	81.47	19.64
c	2	81.70	13.44
c	3	82.18	5.91
c	4	82.32	4.68
c	5	82.45	3.76
c	6	83.23	1.00
d	1	87.49	28.91
d	2	87.70	20.30
d	3	87.74	18.96
d	4	88.00	12.30
d	5	88.14	9.61
d	6	88.21	8.54

Table S2 Energies of compound **1** at B3LYP/6-311+G(d,p) in gas phase.

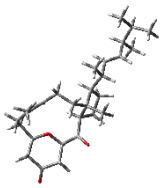
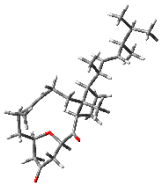
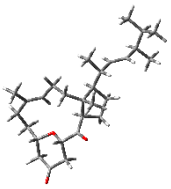
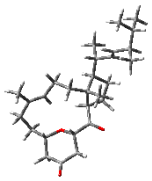
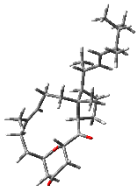
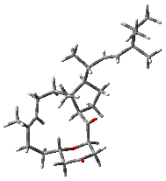
Configuration	Conformer	Structure	E (Hartree)	E (kcal/mol)	Population (%)
a	1		-737.73298391	-462934.43	21.61
a	8		-737.73368179	-462934.87	45.28
b	1		-737.73338632	-462934.69	33.11
b	2		-737.74023312	-462938.98	47.02
c	2		-737.73954070	-462938.55	21.78
d	8		-813.01797551	-510176.48	86.21

Table S3 Standard orientations of compound **1** at B3LYP/6-311+G(d,p) level in gas phase for NMR calculations.

Conformer **a**-1

Center Number	Atomic Number	Atomic Type	Coordinates (Angstroms)		
			X	Y	Z
1	6	0	-4.287038	1.374928	-2.095516
2	1	0	-3.371416	1.400886	-2.693838
3	1	0	-5.109625	1.520789	-2.804505
4	6	0	-4.445072	-0.041134	-1.525426
5	1	0	-4.341547	-0.751779	-2.361835
6	6	0	-5.797210	-0.316899	-0.837413
7	1	0	-6.625628	-0.257404	-1.545812
8	1	0	-5.956327	0.426059	-0.047699
9	6	0	-5.794780	-1.693084	-0.191610
10	6	0	-3.083886	2.802779	-0.218416
11	6	0	-4.301354	2.545144	-1.096956
12	1	0	-5.172636	2.443129	-0.436662
13	1	0	-4.504055	3.464113	-1.664665
14	6	0	-4.566889	-2.000264	0.647778
15	1	0	-4.626911	-1.426097	1.579352
16	1	0	-4.555236	-3.058471	0.906522
17	6	0	-3.286942	-1.585914	-0.093502
18	1	0	-3.106075	-2.292109	-0.924845
19	6	0	-2.028000	-1.623795	0.805670
20	6	0	-1.894082	2.224353	-0.417600
21	1	0	-1.806537	1.536687	-1.249986
22	6	0	-0.758688	-1.023109	0.216955
23	1	0	-1.058618	-0.396472	-0.622591
24	6	0	0.179220	-0.151904	1.125551
25	6	0	-0.469354	1.215652	1.499840
26	1	0	0.129240	1.642217	2.307903
27	1	0	-1.445476	1.004266	1.950912
28	6	0	-0.660187	2.341405	0.439126
29	1	0	0.221199	2.395979	-0.206307
30	1	0	-0.675947	3.286107	0.988189
31	6	0	0.154931	-2.148795	-0.336383
32	1	0	0.151423	-3.004272	0.342711
33	1	0	-0.196562	-2.507060	-1.307174
34	6	0	1.559814	-1.508367	-0.414374
35	1	0	1.931619	-1.465263	-1.439594
36	1	0	2.283133	-2.105864	0.146570
37	6	0	1.450620	-0.084666	0.197918
38	6	0	-3.378768	3.773626	0.899874

39	1	0	-2.489343	4.082171	1.448457
40	1	0	-4.078184	3.333742	1.621554
41	1	0	-3.862113	4.677102	0.509636
42	6	0	0.521981	-0.862752	2.452364
43	1	0	1.263896	-0.284866	3.009178
44	1	0	0.929022	-1.863816	2.295151
45	1	0	-0.362426	-0.971889	3.079367
46	8	0	-6.697979	-2.486240	-0.345072
47	8	0	-2.078091	-2.190094	1.875097
48	8	0	-3.379688	-0.269540	-0.605576
49	6	0	2.811687	0.371635	0.794333
50	6	0	3.887295	0.301751	-0.267297
51	1	0	3.718691	0.927098	-1.146556
52	6	0	2.814640	1.792012	1.395315
53	1	0	3.823254	2.051162	1.726774
54	1	0	2.151407	1.881230	2.256391
55	1	0	2.509240	2.538347	0.655552
56	1	0	3.086676	-0.332889	1.587506
57	1	0	1.212806	0.607061	-0.619793
58	6	0	5.007847	-0.417074	-0.197024
59	6	0	6.084951	-0.469205	-1.252795
60	6	0	7.443768	0.134403	-0.781058
61	6	0	8.031754	-0.550639	0.462236
62	1	0	9.022918	-0.145053	0.684948
63	1	0	8.143672	-1.629454	0.327238
64	1	0	7.406165	-0.383458	1.344180
65	6	0	7.340591	1.649821	-0.563980
66	1	0	6.649917	1.887056	0.250384
67	1	0	6.979575	2.157409	-1.463859
68	1	0	8.316557	2.074401	-0.310374
69	1	0	8.145029	-0.032058	-1.609752
70	1	0	5.751753	0.151762	-2.093984
71	6	0	6.250637	-1.907477	-1.780144
72	1	0	6.512028	-2.605252	-0.979424
73	1	0	7.038091	-1.957767	-2.538726
74	1	0	5.320838	-2.261888	-2.232292
75	1	0	5.167658	-1.043191	0.681411

Conformer **a**-8

Center	Atomic	Atomic	Coordinates (Angstroms)		
Number	Number	Type	X	Y	Z
1	6	0	-4.823003	0.896441	-1.687773
2	1	0	-5.625997	0.995626	-2.427756
3	1	0	-5.290010	1.069213	-0.713735
4	6	0	-4.317016	-0.550539	-1.789115

5	1	0	-3.965010	-0.709297	-2.814150
6	6	0	-5.413029	-1.580602	-1.483370
7	1	0	-5.045036	-2.584546	-1.732608
8	1	0	-6.308022	-1.406450	-2.084336
9	6	0	-5.786041	-1.595951	-0.010377
10	6	0	-2.896996	2.416210	-0.796394
11	6	0	-3.755991	1.983499	-1.970504
12	1	0	-4.286980	2.870592	-2.339296
13	1	0	-3.112988	1.648689	-2.789579
14	6	0	-4.637045	-1.291188	0.935705
15	1	0	-4.755038	-0.259271	1.286951
16	1	0	-4.714058	-1.923399	1.820553
17	6	0	-3.274041	-1.465040	0.261674
18	1	0	-3.116050	-2.540996	0.071418
19	6	0	-2.115045	-1.038275	1.196786
20	6	0	-1.572998	2.216199	-0.802431
21	1	0	-1.159996	1.703402	-1.668551
22	6	0	-0.805036	-0.668128	0.529885
23	1	0	-1.078024	-0.165903	-0.396997
24	6	0	0.207967	0.253683	1.279113
25	6	0	-0.383021	1.678644	1.468450
26	1	0	0.241978	2.215465	2.188583
27	1	0	-1.352026	1.560534	1.966414
28	6	0	-0.573002	2.624936	0.253675
29	1	0	0.393003	2.791043	-0.230278
30	1	0	-0.858996	3.597840	0.667905
31	6	0	0.009955	-1.922038	0.123591
32	1	0	0.006942	-2.663231	0.927414
33	1	0	-0.411042	-2.402822	-0.762528
34	6	0	1.436962	-1.373994	-0.119267
35	1	0	1.738970	-1.484747	-1.162291
36	1	0	2.167952	-1.933142	0.469605
37	6	0	1.437973	0.123905	0.304092
38	6	0	-3.630998	3.120950	0.318769
39	1	0	-2.958000	3.519762	1.077870
40	1	0	-4.332009	2.451834	0.829603
41	1	0	-4.227987	3.952050	-0.076037
42	6	0	0.574951	-0.285655	2.678987
43	1	0	1.363953	0.324230	3.126139
44	1	0	0.936941	-1.316650	2.644743
45	1	0	-0.288054	-0.266806	3.341985
46	8	0	-6.907046	-1.830034	0.381558
47	8	0	-2.298055	-1.079560	2.394774
48	8	0	-3.148025	-0.758746	-0.972156

49	6	0	2.845974	0.566776	0.789209
50	6	0	3.874980	0.287023	-0.283850
51	1	0	3.716992	0.806251	-1.231727
52	6	0	2.950985	2.051678	1.191565
53	1	0	3.976985	2.285598	1.486629
54	1	0	2.298980	2.300484	2.029620
55	1	0	2.692998	2.708881	0.354721
56	1	0	3.107961	-0.041436	1.663066
57	1	0	1.203986	0.722120	-0.585767
58	6	0	4.943971	-0.499019	-0.154029
59	6	0	5.971977	-0.767772	-1.226086
60	6	0	7.392979	-0.230870	-0.872946
61	6	0	7.974963	-0.811186	0.424920
62	1	0	9.005966	-0.473229	0.562009
63	1	0	7.988953	-1.904185	0.419659
64	1	0	7.406960	-0.484390	1.299994
65	6	0	7.421994	1.303122	-0.838578
66	1	0	6.789991	1.692935	-0.035490
67	1	0	7.064005	1.730350	-1.780479
68	1	0	8.439996	1.669072	-0.671483
69	1	0	8.042983	-0.552679	-1.697018
70	1	0	5.656989	-0.226553	-2.126959
71	6	0	5.998965	-2.268688	-1.576445
72	1	0	6.231953	-2.884899	-0.704590
73	1	0	6.748970	-2.477511	-2.345489
74	1	0	5.025965	-2.592588	-1.955530
75	1	0	5.091959	-1.019247	0.792847

Conformer **b**-1

Center	Atomic	Atomic	Coordinates (Angstroms)		
Number	Number	Type	X	Y	Z
1	6	0	-4.463555	1.454625	-1.819385
2	1	0	-3.640500	1.198486	-2.493936
3	1	0	-5.354831	1.543902	-2.449181
4	6	0	-4.675127	0.280108	-0.857656
5	1	0	-5.134240	0.653560	0.071387
6	6	0	-5.569650	-0.837579	-1.428111
7	1	0	-5.148021	-1.161935	-2.388158
8	1	0	-6.590814	-0.491188	-1.598762
9	6	0	-5.609405	-2.037291	-0.493483
10	6	0	-3.016117	3.033817	-0.268165
11	6	0	-4.244462	2.819162	-1.142708
12	1	0	-5.131479	3.029495	-0.529664
13	1	0	-4.256441	3.596143	-1.920014
14	6	0	-4.265508	-2.458723	0.081470

15	1	0	-4.416691	-3.146010	0.912689
16	1	0	-3.713648	-2.984271	-0.707989
17	6	0	-3.444020	-1.222495	0.512620
18	1	0	-3.920200	-0.771003	1.397825
19	6	0	-2.024137	-1.621272	0.957505
20	6	0	-1.910133	2.287180	-0.377577
21	1	0	-1.918321	1.497914	-1.118324
22	6	0	-0.805357	-1.020737	0.268872
23	1	0	-1.154706	-0.395657	-0.550202
24	6	0	0.153535	-0.132647	1.153794
25	6	0	-0.482398	1.243740	1.517987
26	1	0	0.119460	1.668065	2.324661
27	1	0	-1.461672	1.050299	1.971543
28	6	0	-0.655249	2.364847	0.449831
29	1	0	0.211055	2.373775	-0.218417
30	1	0	-0.618576	3.316300	0.984606
31	6	0	0.102455	-2.133899	-0.308604
32	1	0	0.088445	-3.002645	0.351579
33	1	0	-0.259317	-2.464549	-1.285495
34	6	0	1.514360	-1.511550	-0.381727
35	1	0	1.899108	-1.483832	-1.402576
36	1	0	2.226231	-2.108673	0.194619
37	6	0	1.414175	-0.081741	0.212071
38	6	0	-3.184010	4.182213	0.698318
39	1	0	-2.274232	4.423726	1.246837
40	1	0	-3.968463	3.961488	1.432298
41	1	0	-3.503330	5.086618	0.166661
42	6	0	0.503050	-0.831534	2.483665
43	1	0	-0.375915	-0.930575	3.122484
44	1	0	1.248395	-0.249720	3.031506
45	1	0	0.903048	-1.835789	2.334233
46	8	0	-6.639552	-2.612915	-0.220497
47	8	0	-1.934962	-2.449651	1.839913
48	8	0	-3.396064	-0.273930	-0.534353
49	6	0	2.782146	0.379364	0.790328
50	6	0	2.796319	1.804914	1.378936
51	1	0	2.143174	1.904229	2.246780
52	1	0	2.486062	2.546246	0.636220
53	1	0	3.809432	2.062985	1.697271
54	1	0	3.063833	-0.319110	1.586527
55	6	0	3.845684	0.296768	-0.282547
56	1	0	3.670931	0.917846	-1.163614
57	1	0	1.168311	0.598799	-0.612450
58	6	0	4.961585	-0.429978	-0.221088

59	6	0	6.024938	-0.497847	-1.289801
60	6	0	7.397487	0.088320	-0.836100
61	6	0	7.992534	-0.603538	0.399967
62	1	0	8.992026	-0.211363	0.609111
63	1	0	8.087899	-1.683887	0.264594
64	1	0	7.381066	-0.427109	1.289958
65	6	0	7.316564	1.605073	-0.619134
66	1	0	6.639294	1.851448	0.203729
67	1	0	6.950465	2.116442	-1.514818
68	1	0	8.300958	2.017531	-0.378417
69	1	0	8.085755	-0.087879	-1.673612
70	1	0	5.689505	0.125969	-2.127985
71	6	0	6.164636	-1.939188	-1.816556
72	1	0	6.425165	-2.639363	-1.017687
73	1	0	6.942814	-2.001433	-2.583792
74	1	0	5.224975	-2.281303	-2.257605
75	1	0	5.126557	-1.052676	0.658764

Conformer **b**-2

Center	Atomic	Atomic	Coordinates (Angstroms)		
Number	Number	Type	X	Y	Z
1	6	0	5.014636	1.559220	0.517894
2	1	0	4.617129	1.509168	1.535551
3	1	0	6.103216	1.607208	0.620251
4	6	0	4.628748	0.256808	-0.202843
5	1	0	4.273903	0.500383	-1.215627
6	6	0	5.768945	-0.769435	-0.320012
7	1	0	6.143240	-0.991147	0.687370
8	1	0	6.596491	-0.386097	-0.920490
9	6	0	5.264804	-2.061938	-0.945437
10	6	0	3.067081	2.998961	-0.490782
11	6	0	4.553786	2.836676	-0.205606
12	1	0	5.083166	2.887256	-1.166807
13	1	0	4.910611	3.711217	0.355553
14	6	0	3.935770	-2.568876	-0.408654
15	1	0	3.540458	-3.334086	-1.075028
16	1	0	4.118135	-3.035523	0.566595
17	6	0	2.938761	-1.413597	-0.210662
18	1	0	2.617614	-1.042544	-1.201038
19	6	0	1.651879	-1.858174	0.511412
20	6	0	2.132581	2.347556	0.213877
21	1	0	2.478568	1.701950	1.010359
22	6	0	0.795145	-0.808368	1.212254
23	1	0	1.455414	-0.000087	1.518395
24	6	0	-0.351673	-0.171983	0.313904

25	6	0	0.097938	0.998688	-0.605059
26	1	0	-0.779042	1.255259	-1.209490
27	1	0	0.832879	0.620995	-1.324752
28	6	0	0.643788	2.329223	-0.005280
29	1	0	0.137309	2.549158	0.940409
30	1	0	0.352663	3.132620	-0.685264
31	6	0	0.075587	-1.395933	2.462067
32	1	0	0.118027	-2.484818	2.453167
33	1	0	0.584692	-1.056712	3.367551
34	6	0	-1.381372	-0.887216	2.418365
35	1	0	-1.743797	-0.592627	3.406255
36	1	0	-2.045682	-1.675149	2.056803
37	6	0	-1.343236	0.292355	1.435142
38	6	0	2.779873	3.953908	-1.624035
39	1	0	1.718425	4.161868	-1.754749
40	1	0	3.165329	3.561306	-2.572690
41	1	0	3.288845	4.910221	-1.455005
42	6	0	-0.971475	-1.243226	-0.606708
43	1	0	-1.852114	-0.852010	-1.115375
44	1	0	-1.267230	-2.142820	-0.064889
45	1	0	-0.255821	-1.554373	-1.373210
46	8	0	5.876332	-2.641337	-1.816387
47	8	0	1.345368	-3.030674	0.477421
48	8	0	3.537192	-0.347559	0.507516
49	6	0	-2.708981	0.911223	1.019795
50	6	0	-3.232101	1.817516	2.159265
51	1	0	-4.151286	2.324860	1.857593
52	1	0	-2.493111	2.579015	2.426947
53	1	0	-3.454904	1.235550	3.058547
54	1	0	-2.531774	1.558579	0.153074
55	6	0	-3.794808	-0.068994	0.641294
56	1	0	-4.035717	-0.829389	1.383586
57	1	0	-0.816312	1.097554	1.961688
58	6	0	-4.518278	-0.024034	-0.478065
59	6	0	-5.635943	-0.971686	-0.838834
60	6	0	-7.032172	-0.281677	-0.922532
61	6	0	-7.100650	0.864701	-1.943382
62	1	0	-8.126046	1.236265	-2.027538
63	1	0	-6.784645	0.550291	-2.941347
64	1	0	-6.473645	1.708575	-1.639975
65	6	0	-7.509006	0.193994	0.455987
66	1	0	-6.856699	0.977611	0.852298
67	1	0	-7.518652	-0.627378	1.179118
68	1	0	-8.523585	0.599595	0.398806

69	1	0	-7.727398	-1.062248	-1.259493
70	1	0	-5.710703	-1.713621	-0.033867
71	6	0	-5.295855	-1.733340	-2.134588
72	1	0	-5.133066	-1.052241	-2.974999
73	1	0	-6.105022	-2.417000	-2.409820
74	1	0	-4.383918	-2.322208	-2.008232
75	1	0	-4.279692	0.738027	-1.221298

Conformer **c**-2

Center	Atomic	Atomic	Coordinates (Angstroms)		
Number	Number	Type	X	Y	Z
1	6	0	5.127001	1.412097	-0.067004
2	1	0	6.161997	1.749111	0.052996
3	1	0	5.057006	1.071096	-1.105004
4	6	0	4.966018	0.230095	0.903996
5	1	0	5.129013	0.601097	1.919996
6	6	0	5.990034	-0.887891	0.606996
7	1	0	5.975043	-1.597891	1.441996
8	1	0	7.002028	-0.493877	0.502996
9	6	0	5.600044	-1.632896	-0.655004
10	6	0	2.865985	2.569065	-0.577004
11	6	0	4.180985	2.612084	0.176996
12	1	0	4.715972	3.523091	-0.122004
13	1	0	3.986983	2.706081	1.249996
14	6	0	4.159050	-2.097917	-0.676004
15	1	0	4.067062	-2.948918	0.008996
16	1	0	3.899055	-2.450920	-1.674004
17	6	0	3.192035	-0.994930	-0.209004
18	1	0	3.057025	-0.257932	-1.016004
19	6	0	1.790043	-1.568950	0.099996
20	6	0	1.707988	2.409049	0.075996
21	1	0	1.764989	2.317050	1.157996
22	6	0	0.804031	-0.692963	0.854996
23	1	0	1.347019	0.183044	1.202996
24	6	0	-0.453976	-0.185981	0.047996
25	6	0	-0.145992	0.926023	-0.988004
26	1	0	-1.061994	1.080011	-1.569004
27	1	0	0.586014	0.536034	-1.706004
28	6	0	0.324989	2.328030	-0.521004
29	1	0	-0.394017	2.737020	0.193996
30	1	0	0.265980	2.982029	-1.397004
31	6	0	0.203041	-1.428972	2.083996
32	1	0	0.848039	-1.300963	2.955996
33	1	0	0.138056	-2.498973	1.882996
34	6	0	-1.205967	-0.814991	2.300996

35	1	0	-1.974957	-1.576002	2.151996
36	1	0	-1.331973	-0.432993	3.315996
37	6	0	-1.320983	0.312007	1.251996
38	6	0	2.973983	2.750067	-2.072004
39	1	0	2.004983	2.749053	-2.571004
40	1	0	3.579994	1.964075	-2.535004
41	1	0	3.472970	3.699074	-2.305004
42	6	0	-1.121960	-1.342990	-0.721004
43	1	0	-2.056965	-1.010003	-1.172004
44	1	0	-1.342948	-2.197993	-0.081004
45	1	0	-0.469955	-1.704981	-1.519004
46	8	0	6.372047	-1.835886	-1.568004
47	8	0	1.521059	-2.694953	-0.260004
48	8	0	3.646026	-0.332924	0.968996
49	6	0	-2.741991	0.880987	0.981996
50	6	0	-3.212003	1.698981	2.207996
51	1	0	-4.156010	2.205967	1.991996
52	1	0	-2.472013	2.455991	2.483996
53	1	0	-3.373994	1.055978	3.077996
54	1	0	-2.658001	1.582988	0.143996
55	6	0	-3.813977	-0.121028	0.622996
56	1	0	-3.939965	-0.963030	1.301996
57	1	0	-0.761995	1.160015	1.667996
58	6	0	-4.654979	-0.006040	-0.407004
59	6	0	-5.762965	-0.971055	-0.748004
60	6	0	-7.189974	-0.362075	-0.587004
61	6	0	-7.428991	0.896922	-1.434004
62	1	0	-8.472996	1.214907	-1.356004
63	1	0	-7.216989	0.729925	-2.494004
64	1	0	-6.809003	1.730930	-1.093004
65	6	0	-7.523978	-0.092080	0.885996
66	1	0	-6.865988	0.673930	1.307996
67	1	0	-7.411965	-0.996078	1.491996
68	1	0	-8.554982	0.256906	0.993996
69	1	0	-7.882963	-1.135085	-0.944004
70	1	0	-5.704954	-1.804054	-0.036004
71	6	0	-5.548957	-1.557052	-2.157004
72	1	0	-5.528968	-0.776052	-2.923004
73	1	0	-6.349947	-2.258063	-2.415004
74	1	0	-4.598950	-2.095039	-2.212004
75	1	0	-4.530991	0.837962	-1.087004

Conformer **d**-8

Center	Atomic	Atomic	Coordinates (Angstroms)		
Number	Number	Type	X	Y	Z

1	6	0	-5.263936	0.174335	-0.712137
2	1	0	-4.921323	0.530277	-1.686063
3	1	0	-6.216854	-0.333651	-0.892244
4	6	0	-4.230800	-0.828982	-0.188457
5	1	0	-3.498104	-0.283956	0.420719
6	6	0	-4.833189	-1.955148	0.663556
7	1	0	-5.575594	-2.489459	0.056749
8	1	0	-5.331193	-1.568921	1.555323
9	6	0	-3.766210	-2.951070	1.083514
10	6	0	-4.267562	2.229648	0.522950
11	6	0	-5.484587	1.353815	0.247055
12	1	0	-5.848595	0.969169	1.208501
13	1	0	-6.303240	1.977969	-0.133750
14	6	0	-2.789230	-3.340318	-0.015393
15	1	0	-1.903347	-3.785953	0.434179
16	1	0	-3.293595	-4.103768	-0.619997
17	6	0	-2.411775	-2.172128	-0.946971
18	1	0	-2.046682	-2.587359	-1.892727
19	6	0	-1.216916	-1.322408	-0.404943
20	6	0	-3.270890	2.365213	-0.361488
21	1	0	-3.373593	1.861852	-1.319494
22	6	0	-0.927447	-0.016964	-1.139079
23	1	0	-1.867715	0.334105	-1.557917
24	6	0	-0.186469	1.151448	-0.359004
25	6	0	-0.734883	2.530642	-0.857059
26	1	0	-0.886151	2.470081	-1.942526
27	1	0	0.063523	3.265699	-0.717583
28	6	0	-1.994402	3.148539	-0.207207
29	1	0	-2.122346	4.133896	-0.678097
30	1	0	-1.794154	3.352277	0.846564
31	6	0	0.055109	-0.399432	-2.286181
32	1	0	-0.140556	-1.384736	-2.717656
33	1	0	-0.045358	0.329052	-3.097603
34	6	0	1.424363	-0.280342	-1.625408
35	1	0	2.242427	-0.286134	-2.348893
36	1	0	1.589657	-1.114723	-0.937610
37	6	0	1.332138	1.046285	-0.853615
38	6	0	-4.305227	2.913509	1.867129
39	1	0	-3.483962	3.612982	2.018656
40	1	0	-4.285143	2.179334	2.681639
41	1	0	-5.241326	3.473406	1.978618
42	6	0	-0.358078	1.038979	1.166532
43	1	0	0.043461	1.917075	1.676200
44	1	0	0.131040	0.154458	1.567738

45	1	0	-1.416667	0.971896	1.430824
46	8	0	-3.716063	-3.424146	2.196567
47	8	0	-0.490395	-1.801649	0.439390
48	8	0	-3.541891	-1.390762	-1.316656
49	6	0	2.455942	1.248219	0.198986
50	6	0	3.797653	0.808035	-0.340068
51	1	0	4.138160	1.322438	-1.241189
52	6	0	2.576114	2.718165	0.655729
53	1	0	3.345599	2.816859	1.425543
54	1	0	1.642128	3.108815	1.063254
55	1	0	2.864901	3.358596	-0.184883
56	1	0	2.235459	0.625853	1.071703
57	1	0	1.464571	1.842190	-1.599511
58	6	0	4.590313	-0.110317	0.212692
59	6	0	5.948271	-0.517306	-0.305337
60	6	0	7.096965	-0.001760	0.617510
61	6	0	8.475164	-0.159151	-0.042010
62	1	0	8.762464	-1.210491	-0.137827
63	1	0	9.246537	0.334689	0.556545
64	1	0	8.493193	0.286463	-1.041503
65	6	0	7.095885	-0.625949	2.021207
66	1	0	7.302010	-1.699854	1.985069
67	1	0	6.141218	-0.483249	2.533833
68	1	0	7.871809	-0.166906	2.640992
69	1	0	6.915054	1.073537	0.737156
70	1	0	6.090830	-0.016376	-1.271511
71	6	0	5.990005	-2.037160	-0.556198
72	1	0	5.797147	-2.601885	0.360447
73	1	0	6.957324	-2.357626	-0.951294
74	1	0	5.223545	-2.321459	-1.281566
75	1	0	4.242305	-0.624392	1.108946

Table S4 Statistics of Ordinary Least Squares (OLS) linear regression of experimental and computed ^{13}C-NMR chemical shifts.

Configuration	Conformer	CMAD[a]	CLAD[b]	R^2	*RMSE*	*F*	*p* value
a	1	3.0	7.1	0.9959	3.7	6308.18	< 0.01
	8	3.1	7.1	0.9958	3.7	6204.82	< 0.01
	Boltzmann	3.0	7.1	0.9960	3.7	6444.17	< 0.01
b	1	3.0	8.6	0.9952	4.0	5365.31	< 0.01
	2	2.4	7.8	0.9963	3.5	6967.25	< 0.01
	Boltzmann	2.4	7.9	0.9963	3.5	6986.99	< 0.01
c	2	2.7	7.2	0.9960	3.7	6420.17	< 0.01
d	8	3.8	9.0	0.9933	4.7	3855.39	< 0.01

[a] CMAD (corrected mean absolute deviation) = $(1/n)\sum_i^n |\delta_{calc} - \delta_{exp}|$, [b] CLAD (corrected largest absolute deviation) = $\max(|\delta_{calc} - \delta_{exp}|)$, where δ_{calc} and δ_{exp} refer to the calculated and experimental chemical shifts.

Table S5 Experimental and computed ^{13}C NMR chemical shifts.

Position	Experimental	Calculated			
		a	**b**	**c**	**d**
1	35.5	30.3	35.5	37.9	30.7
2	31.2	27.4	30.1	26.5	31.9
3	75.1	77.2	78.5	79.0	71.9
4	43.0	44.0	47.4	46.6	46.4
5	215.2	209.5	207.6	208.2	206.2
6	44.7	41.4	42.3	42.5	37.2
7	77.3	79.5	80.7	76.5	77.9
8	210.7	213.0	214.5	212.9	215.9
9	128.8	126.9	128.7	127.3	124.2
10	133.0	134.5	132.4	137.8	135.2
11	21.7	22.9	21.7	23.1	25.2
12	37.5	39.7	38.5	37.6	43.0
13	45.5	51.6	52.5	52.7	47.8
14	59.6	53.9	51.7	52.9	55.4
15	23.6	28.6	25.4	27.1	30.4
16	26.0	29.8	25.0	20.4	30.1
17	49.0	47.1	49.1	51.5	57.4
18	16.7	15.7	16.9	17.2	13.3
19	14.7	15.5	15.3	13.2	17.1
20	37.4	42.4	39.1	37.5	39.3
21	21.5	18.0	19.8	22.8	20.0
22	134.8	139.4	137.9	136.0	135.6
23	132.6	129.8	130.8	131.4	135.0
24	42.9	44.4	43.8	44.4	43.9
25	33.1	35.1	34.6	35.1	35.8
26	19.7	12.6	12.0	12.9	12.2
27	20.0	19.8	19.1	19.9	19.3
28	17.5	18.6	17.5	17.8	10.3

Table S6 Experimental and computed ^{1}H NMR chemical shifts.

Position	Experimental	Calculated			
		a	**b**	**c**	**d**
1a	2.34	2.18	2.38	2.28	2.26
1b	2.04	2.18	2.01	2.20	1.73
2a	1.79	2.56	2.23	1.80	2.25
2b	1.59	1.47	1.60	1.36	1.69
3	4.11	3.80	3.11	4.13	3.25
4a	2.56	2.48	2.30	2.65	2.23
4b	2.27	1.96	2.14	2.02	2.20
6a	2.97	2.23	2.46	2.35	2.93
6b	2.65	2.20	2.08	2.23	2.28
7	4.07	3.75	3.48	3.75	4.41
9	5.50	5.63	5.84	5.48	5.21
11a	2.19	2.32	2.37	2.26	2.56
11b	1.95	2.16	2.15	1.94	2.08
12a	1.87	1.77	1.88	1.60	1.87
12b	1.82	1.29	1.25	1.35	1.66
14	2.83	3.79	3.95	3.65	3.76
15a	2.00	1.82	1.93	1.77	1.91
15b	1.61	1.52	1.68	1.77	1.48
16a	1.77	1.77	1.77	1.82	1.40
16b	1.41	1.46	1.66	1.73	1.37
17	1.70	2.00	2.10	2.02	1.39
18	0.89	1.14	0.83	0.84	1.09
19	1.58	1.64	1.70	1.69	1.68
20	2.11	2.06	2.19	2.33	2.20
21	1.02	1.12	1.15	1.14	1.10
22	5.22	5.06	5.09	5.25	4.98
23	5.20	5.01	4.94	4.95	5.28
24	1.86	2.02	2.05	2.05	2.05
25	1.46	1.64	1.63	1.61	1.71
26	0.82	0.90	0.93	0.90	0.96
27	0.84	0.96	0.98	0.95	1.06
28	0.92	1.08	1.09	1.08	0.94

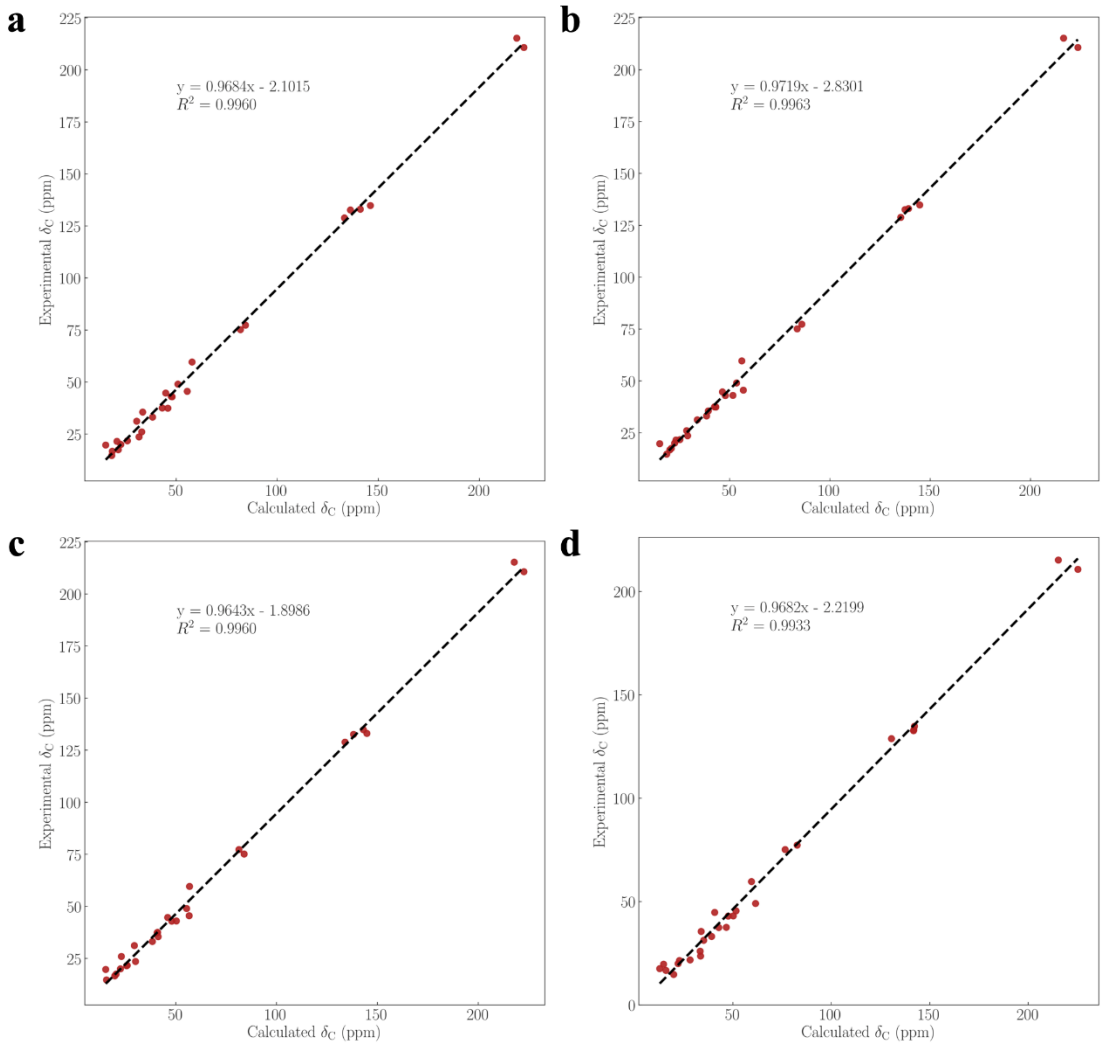


Figure S1 Linear regression fitting of computed ^{13}C NMR chemical shifts of the four configurations **a**–**d** to experimental values.

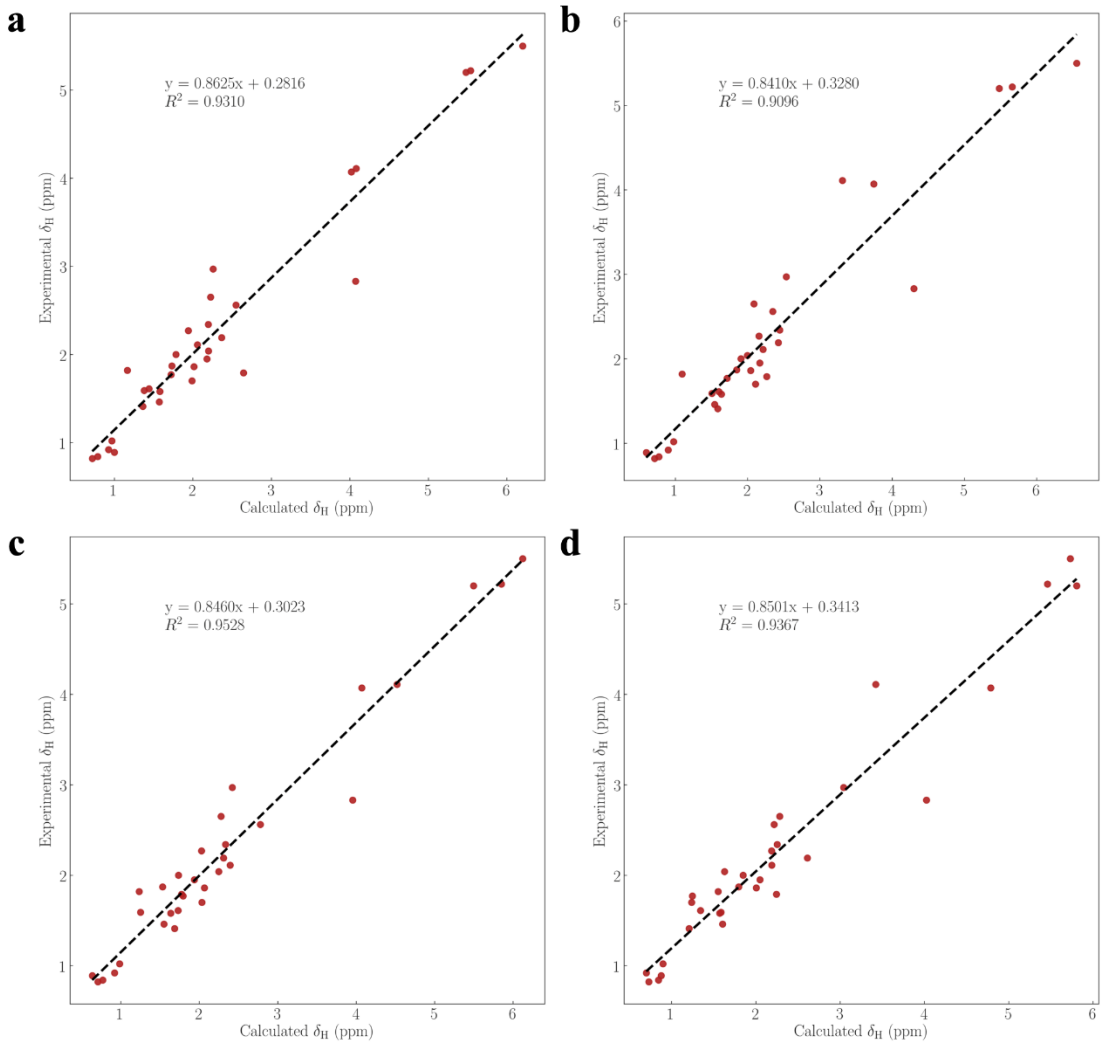
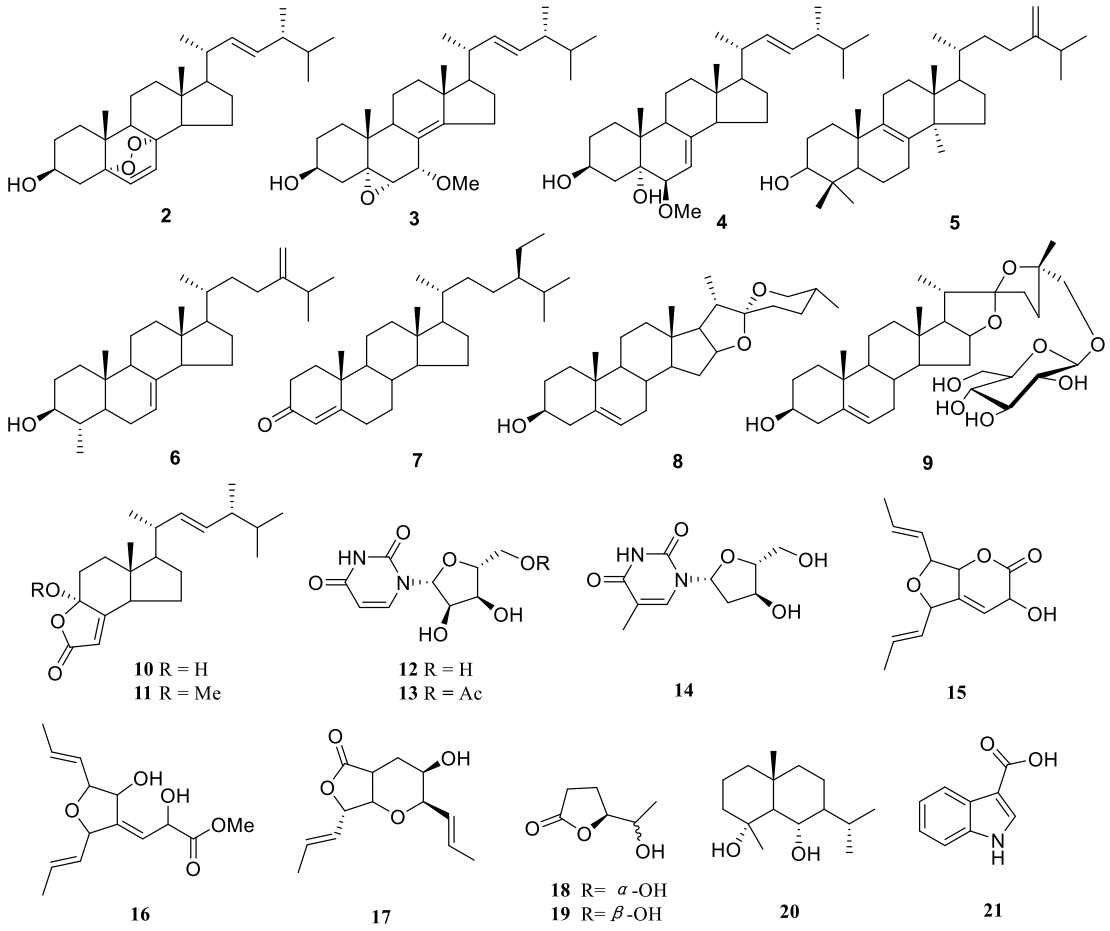


Figure S2 Linear regression fitting of computed ^{1}H NMR chemical shifts of the four configurations **a**–**d** to experimental values.



.**Figure S3**. Chemical structures of all isolated known compounds (**2**–**21**).

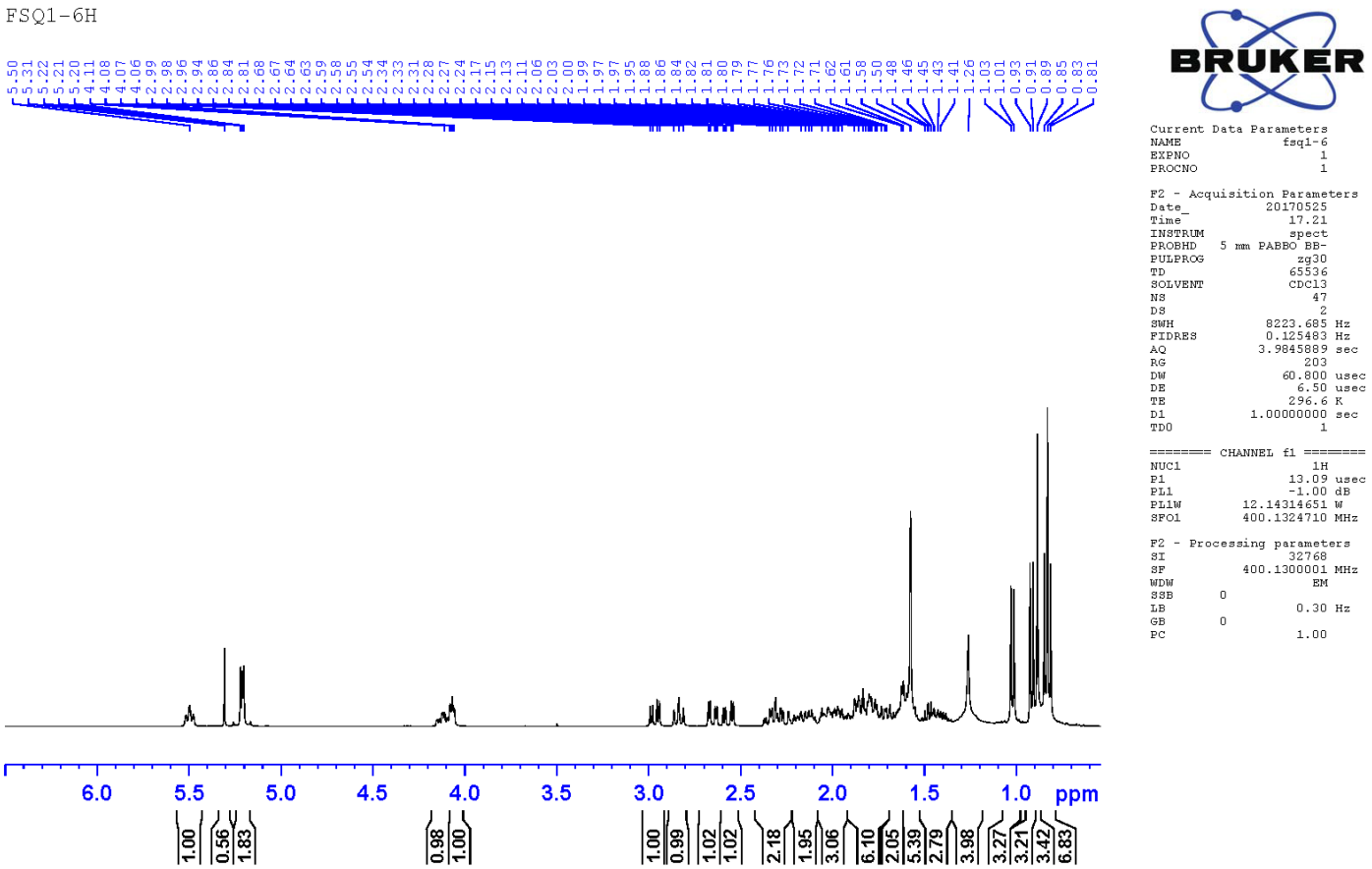



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Figure S4. ^{1}H NMR spectrum of compound **1** in $CDCl_3$.

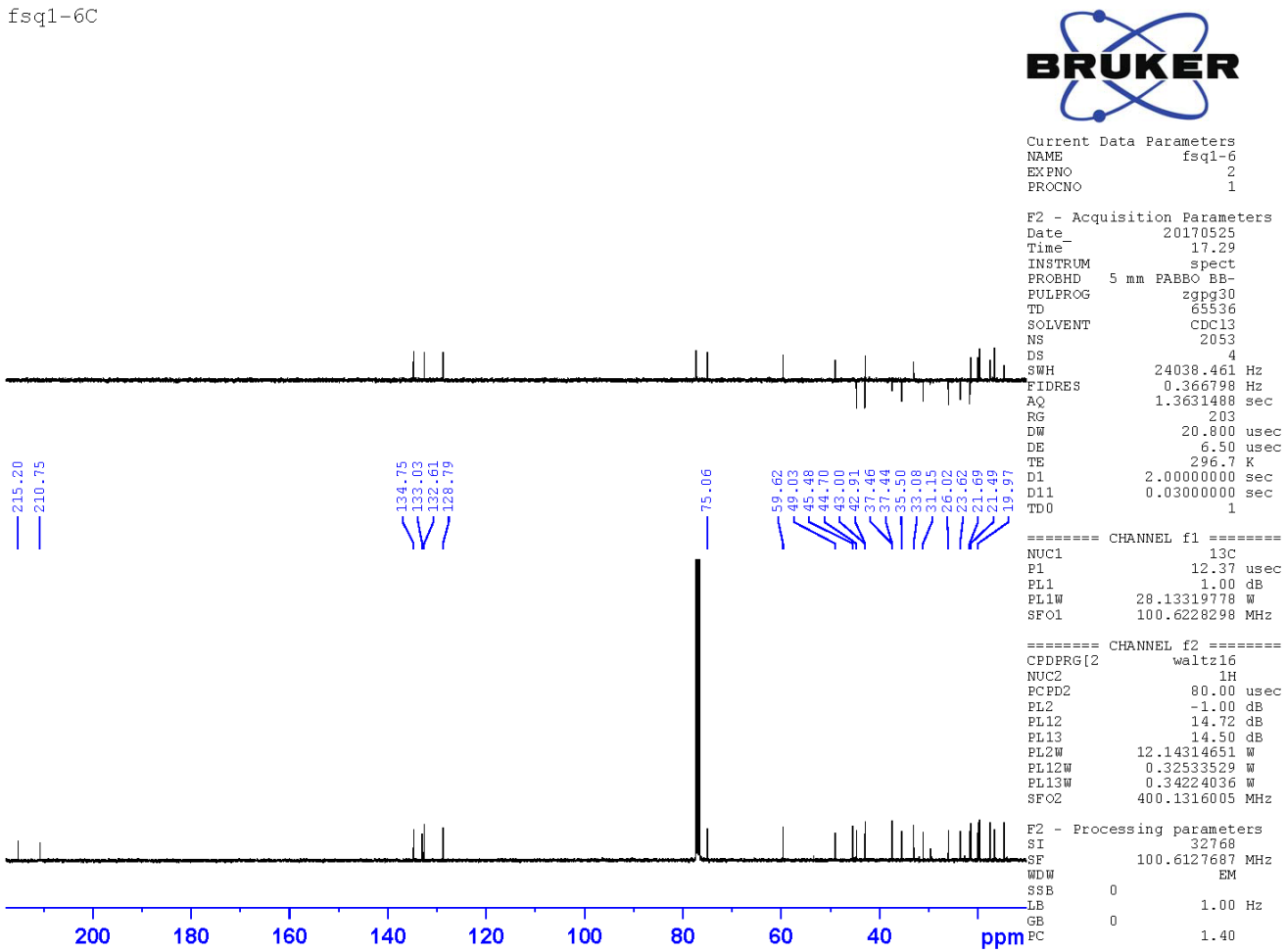


Figure S5. ^{13}C NMR spectrum of compound **1** in $CDCl_3$.

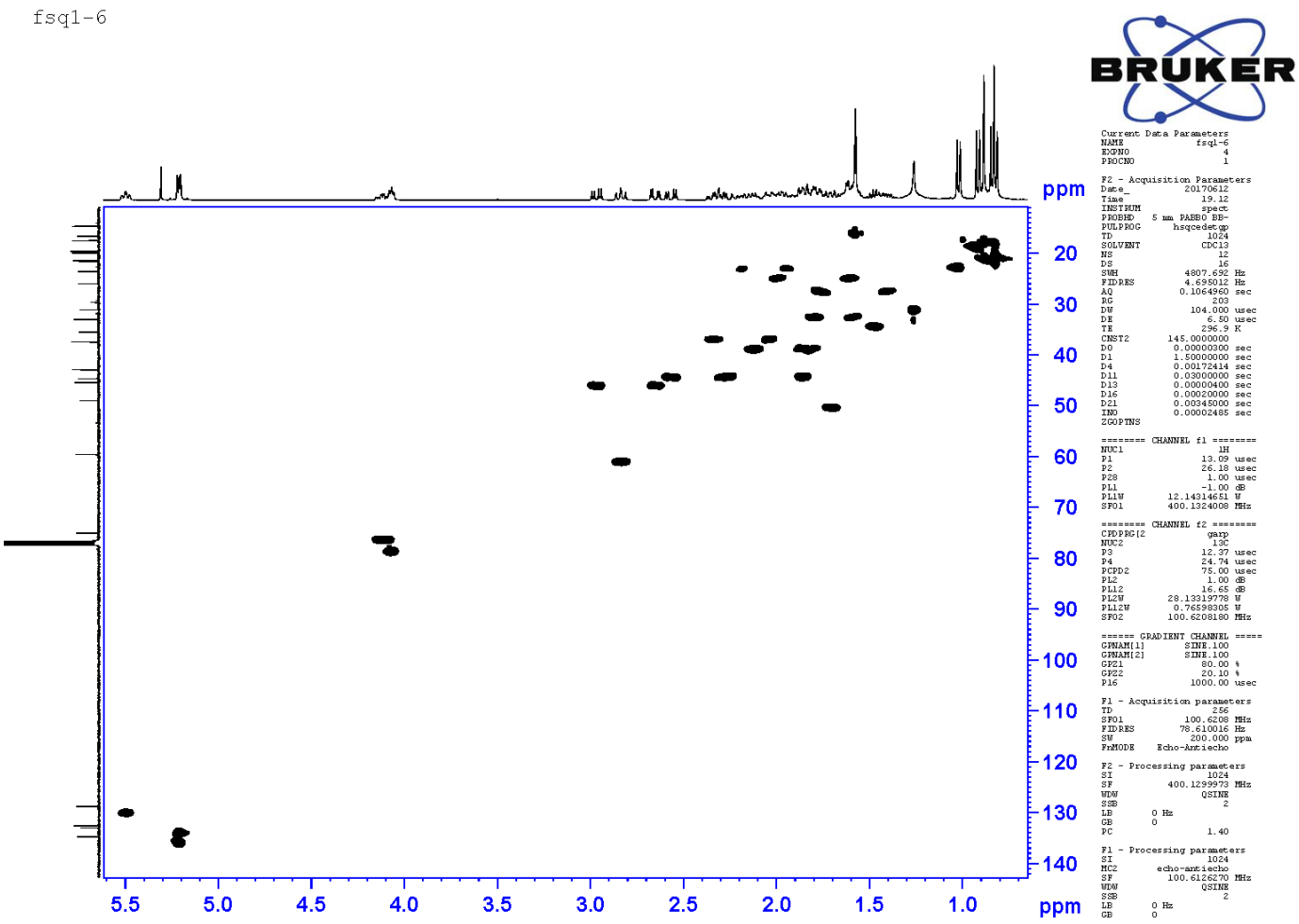


Figure S6. HSQC NMR spectrum of compound **1** in $CDCl_3$.

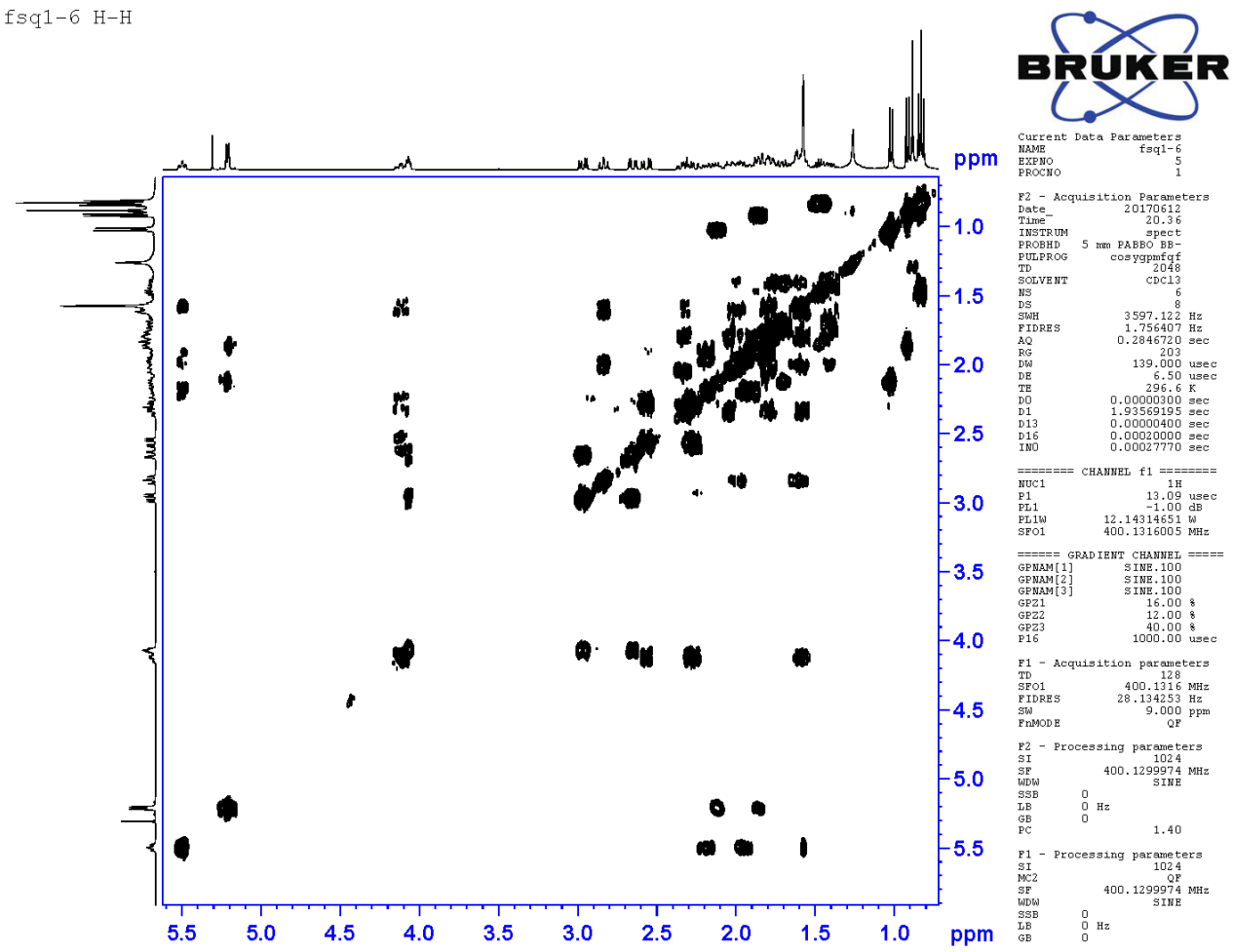


Figure S7. ^{1}H–^{1}H COSY NMR spectrum of compound **1** in $CDCl_3$.

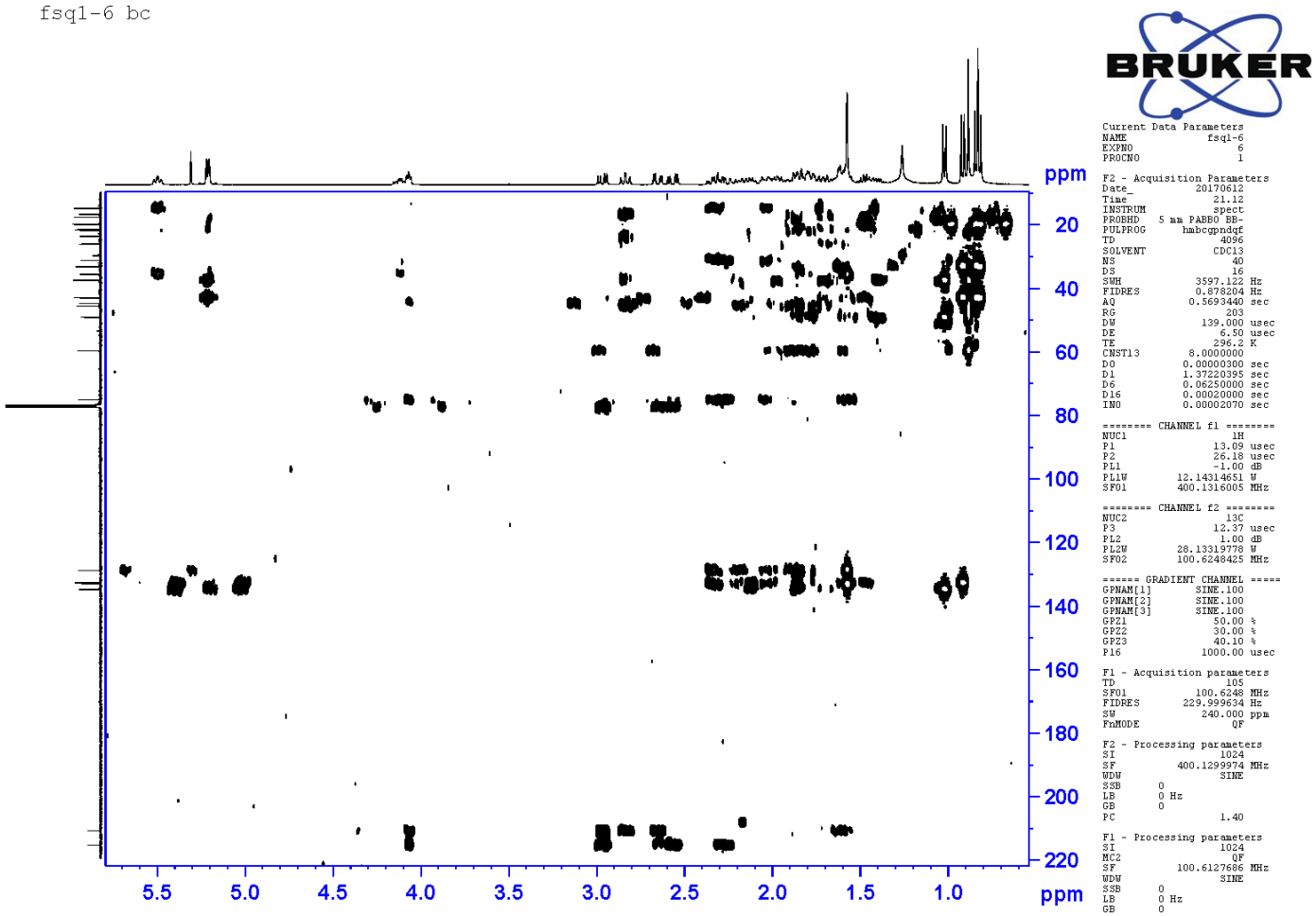
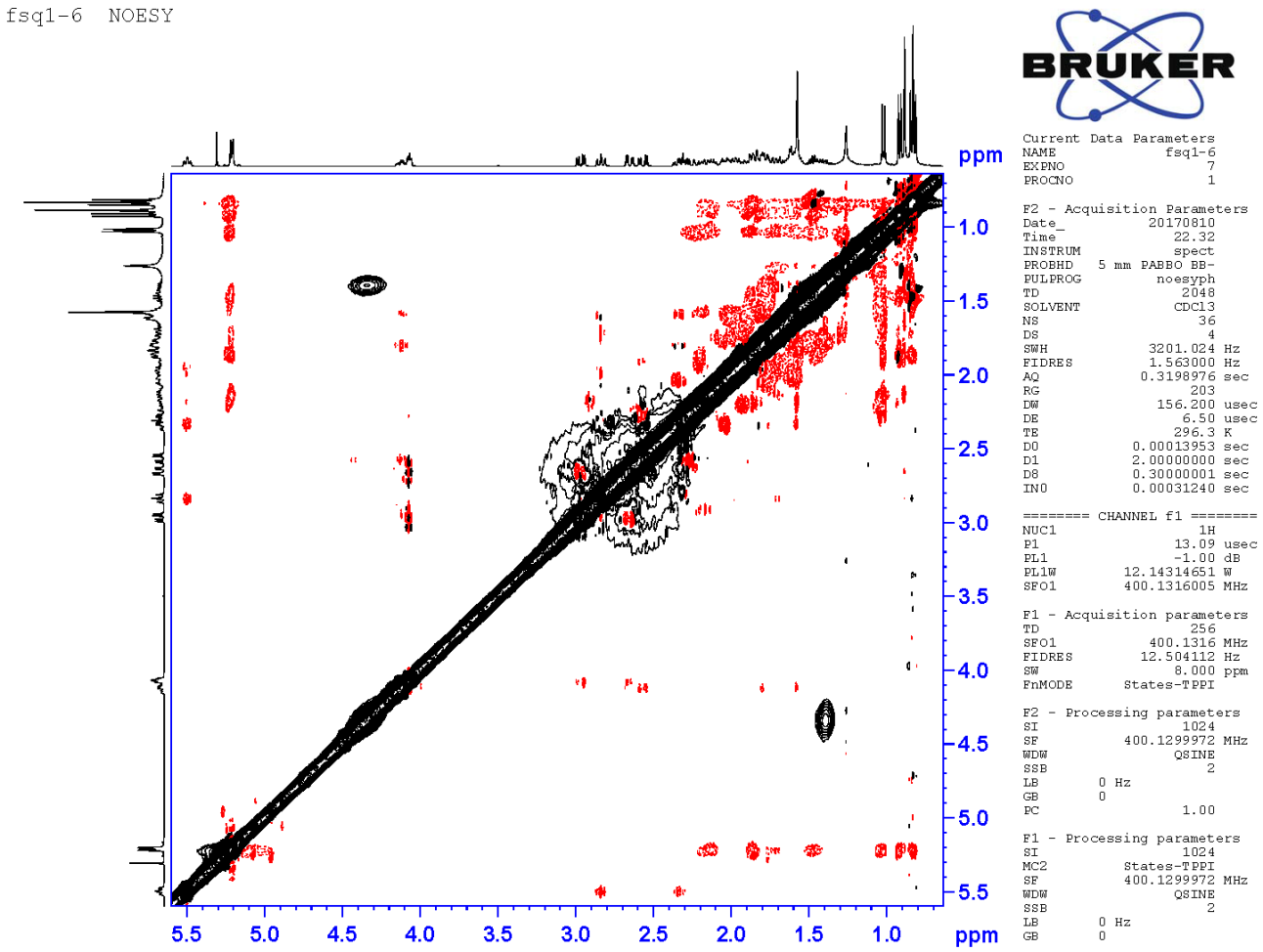


Figure S8. HMBC NMR spectrum of compound **1** in $CDCl_3$.



BRUKER

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DE                   6.50 usec
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IN0               0.00031240 sec

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P1                    13.09 usec
PL1                   -1.00 dB
PL1W          12.14314651 W
SFO1          400.1316005 MHz

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Figure S9. NOESY NMR spectrum of compound **1** in $CDCl_3$.