Supplementary Material (ESI) for Chemical Communications

Neojaponicone A, A Bioactive Sesquiterpene Lactone Dimer with an Unprecedented Carbon Skeleton from *Inula japonica* Thunb.

SUPPORTING INFORMATION

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Experimental Section

General Experimental Procedures. Optical rotations were obtained with a JASCO P-2000 polarimeter. CD spectra were obtained on a JACSO J-815 spectrometer. IR spectra were obtained with a Bruker FTIR Vector 22 spectrometer. ^{1}H and ^{13}C NMR spectra were recorded on Bruker Avance-500 spectrometers using solvent signals ($CDCl_3$: δ_H 7.28/δ_C 77.0) as references. ESIMS spectra were recorded on Varian MAT-212 mass spectrometer. The TOF-ESI spectra were carried out on a Q-Tof micro YA019 mass spectrometer. A preparative column (Shimadzu PRC-ODS EV0233) was used for preparative HPLC (Shimadzu LC-6AD). TLC analysis was run on $HSGF_{254}$ silica gel plates (10-40 μm, Yantai, China). Column chromatography was performed on silica gel (100-200, 200-300 mesh, Yantai, China), silica gel H (10-40 μm, Qingdao, China) and Sephadex LH-20 (Pharmacia Co. Ltd.,).

Plant Material. The aerial parts of *Inula japonica* were collected in Anhui province, PR China, in October, 2006, and were authenticated by Professor Bao Kang Huang, Department of Pharmacognosy, School of Pharmacy, Second Military Medical University. A voucher specimen (No. 2007XFH1) was deposited at School of Pharmacy, Shanghai Jiao Tong University.

Extraction and Isolation. The dried aerial parts of *I. japonica* (20.0 kg) were powdered and extracted with 95% ethanol for three times at room temperature. The ethanolic extract was successively partitioned with petroleum ether (PE), CH_2Cl_2, EtOAc, and *n*-BuOH, respectively. The CH_2Cl_2 fraction (84.5 g) was chromatographed on a silica gel column eluting with a step gradient of CH_2Cl_2-MeOH (100:0, 50:1, 20:1, 10:1, 5:1, 2:1, 1:1) to give 11 fractions (Fr1-Fr11). Fr3 was subjected to a Si gel column chromatography with mixtures of PE-EtOAc (20:1, 10:1, 5:1, 2:1, 1:1, EtOAc) as eluents in a stepwise gradient mode to obtain 9 fractions (Fr3-1–Fr3-9). Subfractions Fr3-5, Fr3-6, and F3-7 were combined and chromatographed on Sephadex LH-20 (CH_2Cl_2/MeOH, 1:1), followed by preparative HPLC (CH_3CN-H_2O, 60:40) to give compound **3** (27.3 mg). By the same procedures, compounds **2** (5.7 mg), **4** (27.2 mg) and **5** (21.0 mg) were obtained from subfraction Fr3-8. Fr4 was subjected to Si gel column chromatography eluted with PE-EtOAc (15:1, 10:1, 5:1, 2:1, 1:1, EtOAc) to give 7 fractions (Fr4-1–Fr4-7). Subfractions Fr4-6 was subjected to preparative HPLC (CH_3CN-H_2O, 35:65) to afford compounds **1** (3.0 mg).

Japonicone M (2). White amorphous powder; $[\alpha]_D^{20}$ +84º (*c* 0.29, $CHCl_3$); IR (KBr) ν_{max} 3500, 2925, 2852, 1765, 1712, 1662, 1435, 1373, 1296, 1234, 1166, 1125, 1083, 1049, 1028, 982, 955 cm^{-1}; for ^1H and ^{13}C NMR data, see Tables 1 and 2; ESIMS (positive) *m/z* 619 $[M+Na]^+$; ESIMS (negative) *m/z* 595 $[M-H]^-$, 631 $[M+Cl]^-$; HRESIMS (positive) $[M+Na]^+$ *m/z* 619.2880 (calcd for $C_{34}H_{44}O_9Na$, 619.2883).

Japonicone N (3). White amorphous powder; $[\alpha]_D^{20}$ +85º (*c* 0.50, $CHCl_3$); IR (KBr) ν_{max} 3485, 3066, 2915, 2848, 1763, 1723, 1663, 1460, 1378, 1347, 1230, 1162, 1028, 981 cm^{-1};for ^1H and ^{13}C NMR data, see Tables 1 and 2; ESIMS (positive) *m/z* 647 $[M+Na]^+$; ESIMS (negative) *m/z* 623 $[M-H]^-$; HRESIMS (positive) $[M+Na]^+$ *m/z* 647.3198 (calcd for $C_{36}H_{48}O_9Na$, 647.3196).

Japonicone O (4). White amorphous powder; $[\alpha]_D^{20}$ +81º (*c* 0.50, $CHCl_3$); IR (KBr) ν_{max} 3504, 2960, 2928, 1768, 1726, 1658, 1459, 1379, 1296, 1232, 1167, 1124, 1029, 983, 905 cm^{-1}; for ^1H and ^{13}C NMR data, see Tables 1 and 2; ESIMS (positive) *m/z* 661 $[M+Na]^+$; ESIMS (negative) *m/z* 637 $[M-H]^-$; HRESIMS (positive) $[M+Na]^+$ *m/z* 661.3354 (calcd for $C_{37}H_{50}O_9Na$, 661.3353).

Japonicone P (5). White amorphous powder; $[\alpha]_D^{20}$ +81° (*c* 0.50, $CHCl_3$); IR (KBr) ν_{max} 3521, 2959, 2931, 2873, 1768, 1731, 1658, 1461, 1376, 1294, 1232, 1168, 1120, 1085, 1029, 983, 912 cm^{-1}; for ^1H and ^{13}C NMR data, see Tables 1 and 2; ESIMS (positive) *m/z* 661 $[M+Na]^+$; ESIMS (negative) *m/z* 637 $[M-H]^-$; HRESIMS (positive) $[M+Na]^+$ *m/z* 661.3355 (calcd for $C_{37}H_{50}O_9Na$, 661.3353).

Biological Activity

Inhibitory activities against lipopolysaccharides (LPS)-induced nitric oxide (NO) production in RAW264.7 macrophages. RAW264.7 macrophages were seeded in 24-well plates (10^5 cells/well). The cells were co-incubated with drugs and LPS (1μg/mL) for 24h. The amount of NO was assessed by determined the nitrite concentration in the cultered RAW264.7 macrophage supernatants with Griess reagent. Aliqueots of supernatants (100 μL) were incubated, in sequence, with 50 μL 1% sulphanilamide and 50 μL 1% naphthylethylenediamine in 2.5% phosphoric acid solution. The absorbances at 570 nm were read using a microtiter plate reader.

MTT assay for cytotoxic activity in RAW264.7 macrophages. RAW264.7 macrophages were maintained in a water-saturated atmospheere of 5% CO_2 at 37 ℃. Experiments were carried out according to the reported protocol. The cell viability was evaluated by MTT [3-(4,5-dimethylthiazol-2-yl)-2,5-diphenyltetrazolium bromide, Sigma] reduction.

Reference:

(a) Denizot, F.; Lang, R. *J. Immunol. Methods* **1986**, *89*, 271–277.

(b) Qin, J. J.; Jin, H. Z.; Zhu, J. X; Fu, J. J.; Hu, X. J.; Liu, X. H.; Zhu, Y.; Yan, S. K.; Zhang, W. D. *Planta Med.* **2010**, *76*, 278–283.

Computational Methods

Original ECD data calculations

The energies, oscillator strengths and rotational strengths of the electronic excitations of all the configurational isomers are calculated using the TDDFT methodology at B3LYP/3-21G level. Rotational strengths are calculated using both length and velocity representations using Gaussian 03 software package.

ECD simulation

The ECD spectra were then simulated by overlapping Gaussian functions for each transition according to:

$$\Delta\varepsilon(E) = \frac{1}{2.297\times10^{-39}} \times \frac{1}{\sqrt{2\pi\sigma}} \sum_{i}^{A} \Delta \mathrm{E}_i R_i e^{-[(E-E_i)/(2\sigma)]^2}$$

Where σ is the width of the band at 1/e height and ΔE_i and R_i are the excitation energies and rotatory strengths for transition i, respectively, σ=0.20 eV and $R^{velocity}$ have been used in this work.

Fig. S1. Key NOESY correlations (⤻) for neojaponicone A (**1**).

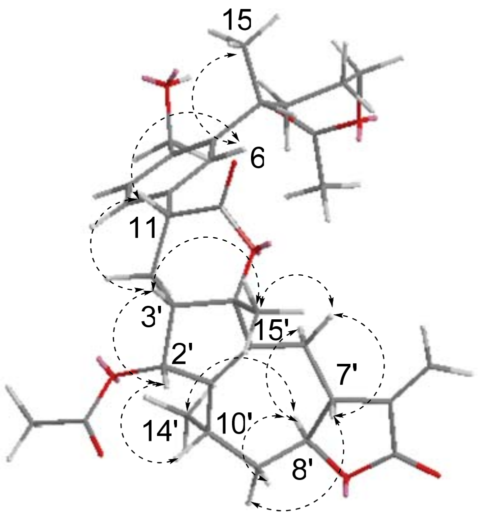

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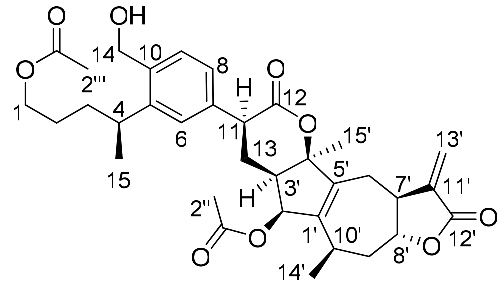
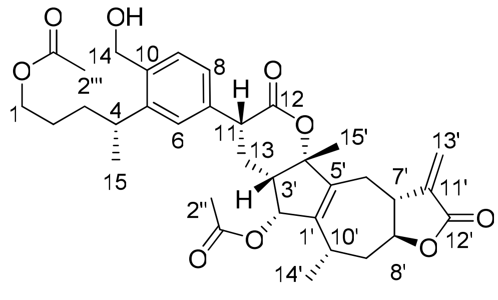
Fig. S2. Four possible configurations of neojaponicone A (**1**).



1-1



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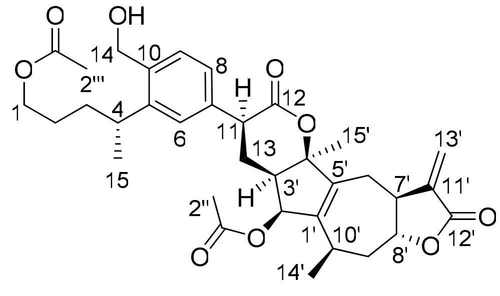
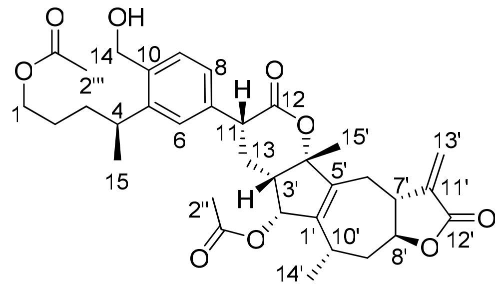
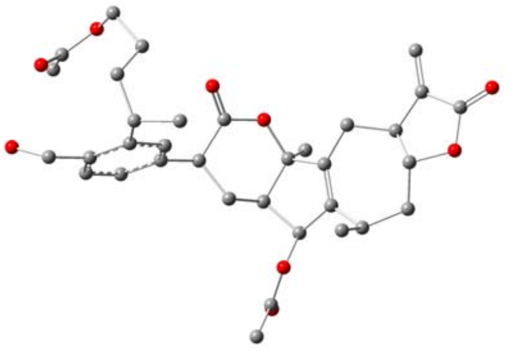


2-1

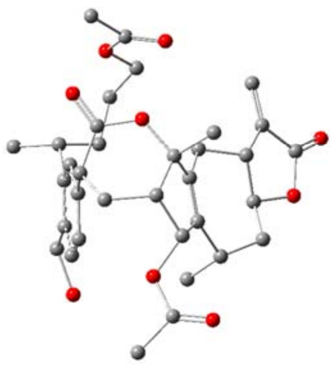


2-2

Fig. S3. Optimized geometries of configurations of neojaponicone A (**1**) at B3LYP/3-21G level in the gas phase.



1-1



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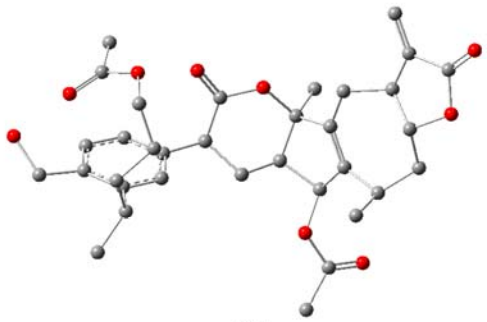
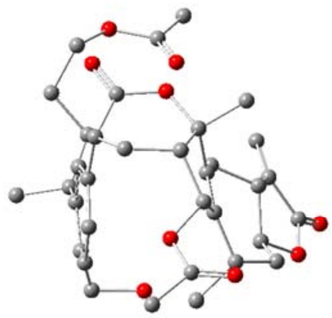


2-1



2-2

Fig. S4. Calculated ECD spectra of configurational isomers of neojaponicone A (**1**) at B3LYP level(—at B3LYP/3-21G level in the gas; —at B3LYP-SCRF/3-21G// B3LYP/3-21G level with COSMO model in MeOH;—experimental in MeOH)

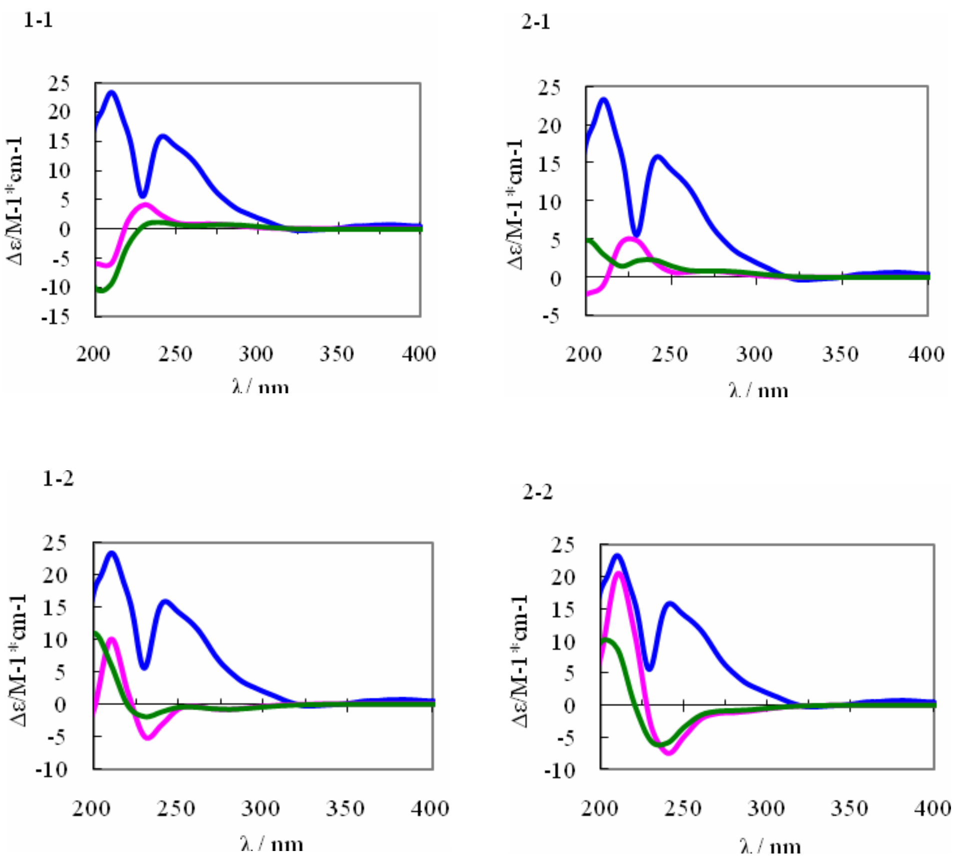
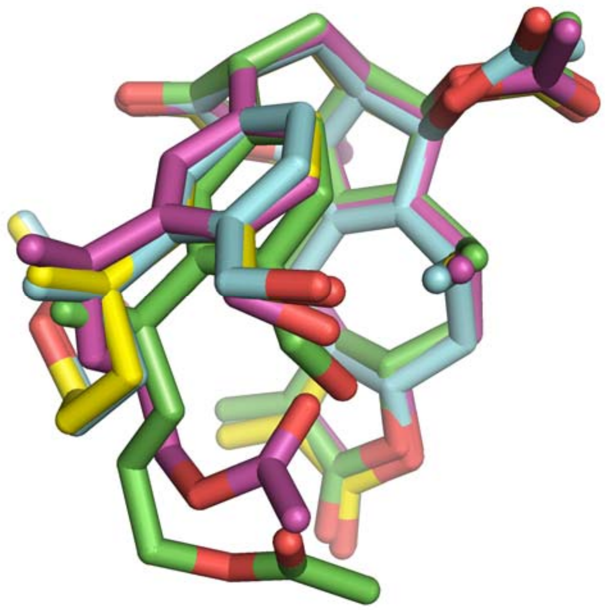


Fig. S5. Optimized geometries of representative 4 conformations of 1-2 from restraint conformation analysis at B3LYP/3-21G level in the gas phase. The conformational search was performed with torsion search method implemented in MacroModel, in which only the single bonds highlighted in red were free to rotate.



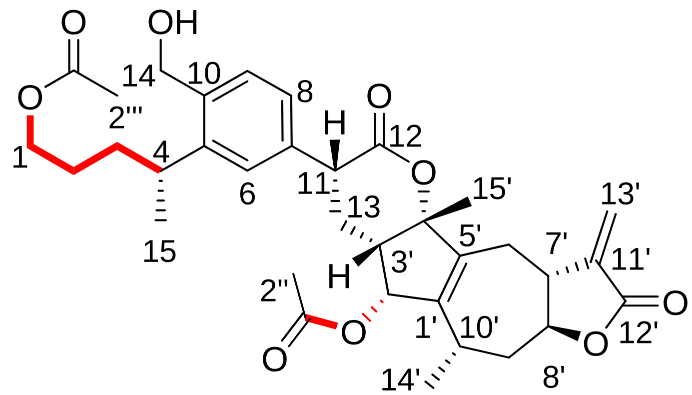


Fig. S6. Calculated ECD spectra of selected conformers of 1-2 (—experimental in MeOH ;—the initial conformer; —, —, —, and — represent conformers 1 to 4. All the computations are performed at B3LYP-SCRF/3-21G// B3LYP/3-21G level with COSMO model in MeOH;)

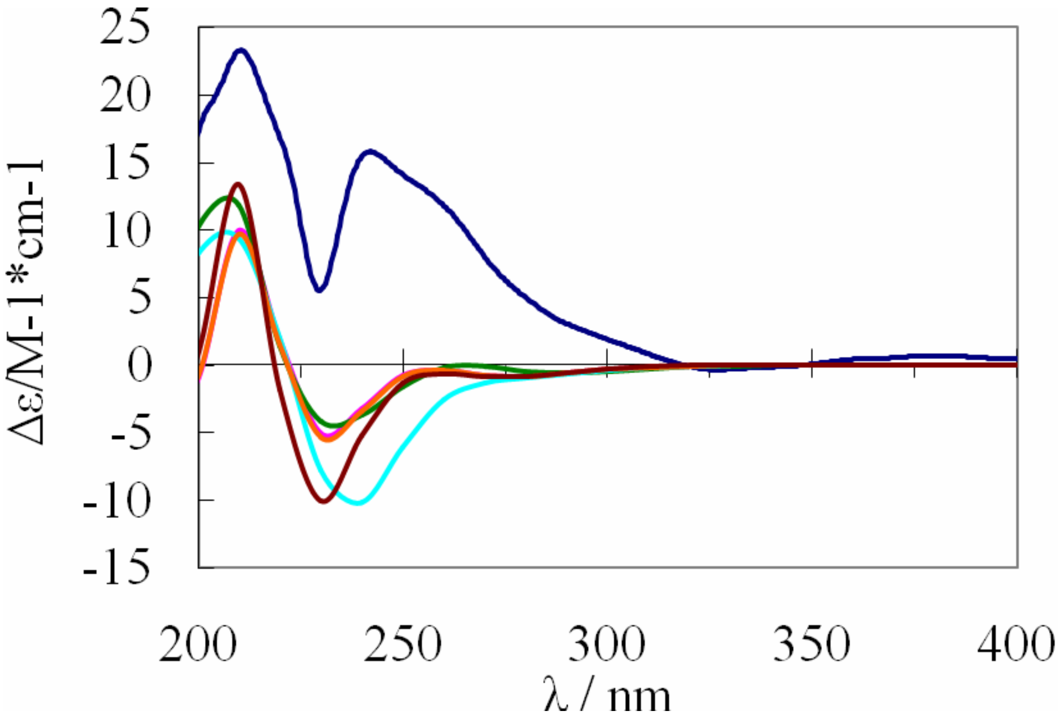


Fig. S7. Some molecular orbitals involved in key transitions in ECD of the configurational isomer 1-2 of neojaponicone A (**1**) at B3LYP-SCRF/3-21G//B3LYP/3-21G level with COSMO model in MeOH.

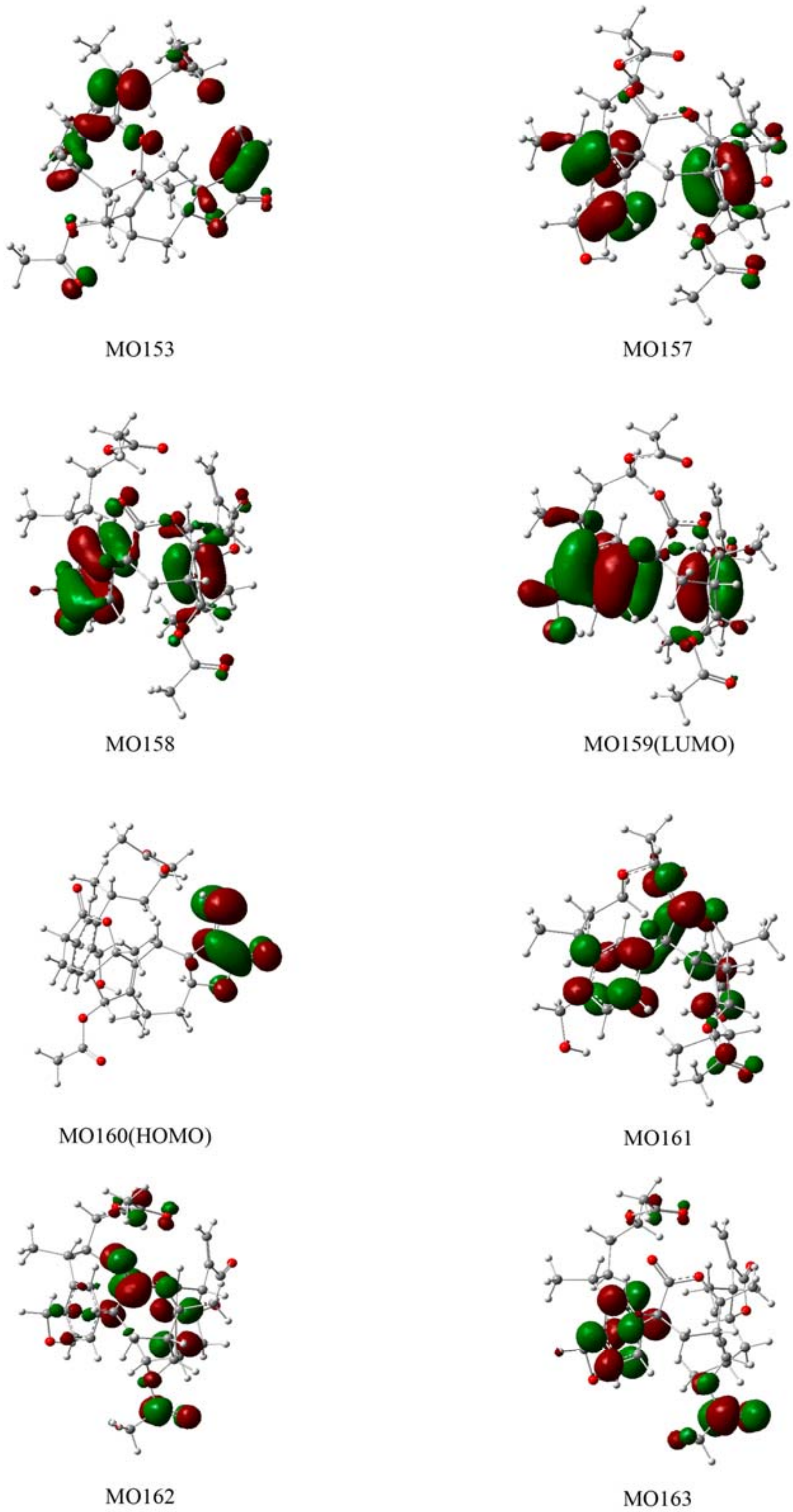


Table S1. Important Dihedral Angles (Degree) and Thermodynamic Parameters (au) of the Optimized neojaponicone A (**1**) at B3LYP/3-21G Level in the Gas Phase.

	E	***E′=E+ZPE***	***H***	***G***	E_{sol}	G_{sol}
1-1	-1987.025952	-1986.307899	-1986.265304	-1986.385652	-1987.068831	-1987.037662
1-2	-1987.018593	-1986.299682	-1986.257281	-1986.373187	-1987.059409	-1986.994242
2-1	-1987.026726	-1986.308161	-1986.265772	-1986.384030	-1987.069354	-1987.035575
2-2	-1987.010525	-1986.291532	-1986.248966	-1986.365695	-1987.052545	-1987.022155

	C6-C5-C4-C15	C8-C7-C11-C12	C11-C13-C3'-C2'	C13-C3'-C2'-O
1-1	-27.91	-102.24	167.93	29.51
1-2	-118.54	28.93	-102.83	-18.70
2-1	-125.55	-151.21	171.79	30.15
2-2	-103.11	25.68	-103.34	-19.87

	C15'-C4'-C5'-C1'	C5'-C1'-C10'-C14'	C13'-C11'-C7'-C8'	C11'-C7'-C8'-O
1-1	-101.44	86.63	-155.57	-31.73
1-2	98.67	-88.58	154.70	32.83
2-1	-102.14	89.12	-155.47	-31.82
2-2	96.78	-94.73	156.04	33.10

E, E′, H, G: total energy, total energy with zero point energy (ZPE), enthalpy and Gibbs free energy in the gas phase at B3LYP/3-21G level;

E_{sol}, G_{sol}: total energy and Gibbs free energy in methanol solution at B3LYP-SCRF/3-21G//B3LYP/3-21G level with COSMO model.

Table S2. Key Transitions, Oscillator Strengths, and Rotatory Strengths in the ECD Spectra of the configurational isomer **1-2** of neojaponicone A (**1**) in the MeOH with COSMO at B3LYP-SCRF/3-21G//B3LYP3-21G Level

Exited State	***ΔE**[a]**(eV)***	***λ**[b]**(nm)***	***f**[c]*	***R_{vel}**[d]*	***R_{len}**[e]*
159 ->160	4.4567	278.2	f=0.0004	-4.5624	0.1505
159 ->160	5.1038	242.93	f=0.0002	0.6519	0.7131
158 ->160	5.1976	238.54	f=0.0106	0.4827	2.9985
157 ->160	5.283	234.68	f=0.0002	1.8086	4.7267
158 ->161	5.3634	231.17	f=0.0009	-0.2409	-0.2317
153 ->161	5.3779	230.54	f=0.0034	-2.5455	-1.3993
159 ->161	5.4588	227.13	f=0.0091	-10.7785	-16.4414
159 ->162	5.5175	224.71	f=0.0008	-0.4299	-0.764
154 ->160	5.5364	223.94	f=0.0021	-3.567	-6.0715
159 ->162	5.5666	222.73	f=0.0015	5.222	7.4819
156 ->160	5.6622	218.97	f=0.0065	5.2548	8.8263
154 ->165	5.672	218.59	f=0.0080	-1.6621	4.6814
152 ->160	5.7321	216.3	f=0.0121	-0.1126	3.2577
158 ->162	5.7816	214.45	f=0.0099	-2.3811	-4.9041
157 ->161	5.8351	212.48	f=0.0220	1.5258	8.121
159 ->163	5.8864	210.63	f=0.0633	-24.3229	-32.3539
153 ->160	5.9054	209.95	f=0.0117	7.4325	8.002
158 ->162	5.9402	208.72	f=0.0051	3.7077	8.2658
157 ->162	5.95	208.38	f=0.0119	8.8358	14.1112
159 ->165	5.9798	207.34	f=0.0038	-7.5414	-7.7912
150 ->160	6.0005	206.62	f=0.0041	7.7761	8.3645

158 ->163	6.0183	206.01	f=0.0014	4.4499	5.099
158 ->166	6.0492	204.96	f=0.0095	7.8558	10.6048
151 ->160	6.1118	202.86	f=0.0116	-5.2246	-6.3667
158 ->163	6.1516	201.55	f=0.0062	2.6434	2.9883
156 ->161	6.1565	201.39	f=0.0044	2.9193	4.8986
148 ->160	6.1779	200.69	f=0.0121	17.194	19.3586
150 ->160	6.2376	198.77	f=0.0349	-31.6366	-27.7885
158 ->165	6.2427	198.61	f=0.0097	44.5107	53.0016
156 ->163	6.2515	198.33	f=0.0015	4.3093	3.8647

[a] Excitation energy. [b] Wavelength. [c] Oscillator strength. [d] Rotatory strength in velocity form (10^{-40}cgs.) [e] Rotatory strength in length form (10^{-40}cgs.).

Table S3. Optimized Z-Matrixes of neojaponicone A (**1**) in the Gas Phase(Å) at B3LYP/3-21G level

1-1				1-2			
C	-4.754101	-1.635907	-0.367923	C	-0.220051	2.930277	-0.071333
C	-5.233189	-1.092353	0.998796	C	0.429985	2.930488	-1.475409
O	-6.479672	-1.862530	1.284270	O	-0.045895	4.199109	-2.100848
C	-6.397778	-3.107212	0.640963	C	-1.290350	4.531708	-1.541411
C	-5.229472	-3.070705	-0.298636	C	-1.528432	3.640058	-0.361063
C	-3.257150	-1.408661	-0.599544	C	-0.269325	1.524592	0.550915
C	-2.905843	0.050547	-0.767335	C	1.109856	1.018922	0.918996
C	-3.352510	1.140264	-0.119268	C	2.242348	0.997188	0.193315
C	-4.310830	1.305300	1.045524	C	2.573952	1.542625	-1.188083
C	-5.562357	0.390588	1.026089	C	1.947649	2.926413	-1.501057
C	-1.915575	0.439202	-1.870076	C	1.402129	0.601459	2.362383
C	-1.447515	1.858533	-1.451360	C	2.735232	-0.200315	2.283133
C	-2.688902	2.387951	-0.687541	C	3.379940	0.377204	0.989211
O	-0.865174	-0.610599	-1.940645	O	0.276944	-0.118896	3.006133
C	0.426863	-0.476811	-1.446971	C	0.091087	-1.469053	2.868749
C	0.899515	0.957831	-1.216085	C	1.090037	-2.245830	2.031361
C	-0.227769	1.762726	-0.524062	C	0.588010	-2.319289	0.571752
C	2.194567	1.002821	-0.432468	C	1.444806	-2.532822	-0.510031
C	3.243442	1.838887	-0.827354	C	0.910724	-2.742618	-1.780050
C	4.431432	1.853676	-0.098344	C	-0.467399	-2.715694	-2.021396
C	4.604475	1.038367	1.025309	C	-1.347206	-2.486426	-0.943112
C	3.556582	0.186308	1.432157	C	-0.792074	-2.322712	0.333041
C	2.360743	0.209055	0.706696	C	-0.913732	-2.974170	-3.458179

C	5.969225	1.123896	1.711597	C	-3.823121	-0.883556	3.353907
C	5.910669	-0.534394	-2.556929	C	-3.315503	-1.119566	-1.874890
C	4.578203	-2.052883	1.914393	C	-2.872064	-2.364144	-1.041531
C	3.768294	-0.864611	2.525114	C	-3.781985	0.069932	2.189611
C	5.952229	-1.398940	-1.320913	C	-4.347197	-0.503299	1.060369
O	5.073164	-2.429017	-1.432446	O	-4.498220	0.375225	-0.135780
C	4.875774	-3.365873	-0.279887	C	-4.647675	-0.501788	-1.382284
C	3.872758	-2.797382	0.743907	C	0.160747	-2.742831	-4.425560
O	7.037324	1.339216	0.746803	O	-3.302379	1.204524	2.195553
C	2.466623	-1.361779	3.192306	C	-2.711872	3.601113	0.246833
O	6.654417	-1.193592	-0.319267	O	-2.005027	5.404339	-2.003153
C	-4.797102	-4.163885	-0.918587	C	2.257438	0.497279	-2.290790
O	-7.178215	-4.016130	0.860628	O	-0.888843	-1.991995	3.398891
C	-3.509773	1.175855	2.373624	C	1.537214	1.855024	3.245240
O	1.085172	-1.491900	-1.273605	O	4.073870	-0.694277	0.208723
C	-2.578226	0.417308	-3.255219	C	5.322698	-0.367643	-0.327394
O	-2.317920	3.291889	0.430025	O	5.940533	-1.602095	-0.940179
C	-2.283505	4.657429	0.124237	C	5.786998	0.765016	-0.294722
C	-1.917243	5.431314	1.367291	C	2.530395	-1.740376	2.287031
O	-2.519374	5.087903	-0.995637	O	-3.556551	-3.658162	-1.543536
H	-5.327246	-1.120565	-1.152682	H	0.382165	3.588074	0.572713
H	-4.505074	-1.356229	1.773628	H	0.018024	2.103302	-2.064697
H	-2.918796	-1.946397	-1.491008	H	-0.911145	1.507382	1.438229
H	-2.694267	-1.833188	0.243624	H	-0.720692	0.828106	-0.169649
H	-4.677727	2.338875	1.004762	H	3.660661	1.695544	-1.195276
H	-6.189823	0.626810	0.158822	H	2.271020	3.232724	-2.502821

H	-6.149695	0.592959	1.929103	H	2.315695	3.674101	-0.788934
H	-1.212752	2.480061	-2.320834	H	3.361898	0.062544	3.140137
H	-3.347764	2.957395	-1.350433	H	4.149147	1.121449	1.215029
H	1.069189	1.399207	-2.209841	H	1.028142	-3.271130	2.416825
H	0.142759	2.761907	-0.284233	H	2.517492	-2.490362	-0.382070
H	-0.505199	1.275768	0.415811	H	1.555594	-2.916975	-2.632117
H	3.137682	2.462916	-1.709886	H	-1.468460	-2.210673	1.170244
H	5.276643	2.457675	-0.405562	H	-1.804215	-2.383762	-3.699366
H	1.560691	-0.459278	0.991163	H	-1.164754	-4.031759	-3.583594
H	5.982576	1.999705	2.370059	H	-2.810215	-1.267879	3.534245
H	6.149227	0.238152	2.330345	H	-4.137231	-0.336110	4.247199
H	6.876616	-0.048170	-2.701889	H	-4.504743	-1.707430	3.147221
H	5.631400	-1.130394	-3.425479	H	-2.535211	-0.349197	-1.821158
H	5.149021	0.238330	-2.395306	H	-3.423525	-1.400571	-2.929334
H	5.527360	-1.666191	1.540208	H	-3.226650	-2.177301	-0.024183
H	4.802461	-2.769550	2.716241	H	-3.633094	1.036700	-0.211813
H	4.388033	-0.423938	3.315024	H	-5.392689	0.986587	0.023764
H	4.485867	-4.256692	-0.772521	H	-5.387863	-1.284966	-1.183322
H	5.849137	-3.573848	0.172797	H	-5.055863	0.140867	-2.173588
H	3.278106	-3.631384	1.135391	H	0.360388	-1.766624	-4.400734
H	3.187637	-2.144981	0.190909	H	-2.932780	2.946302	1.081798
H	7.101181	0.470861	0.241755	H	-3.505360	4.239742	-0.135033
H	1.879053	-0.523278	3.582245	H	2.538387	0.891801	-3.274546
H	2.717266	-2.025978	4.027159	H	2.822730	-0.415410	-2.093430
H	1.844253	-1.927313	2.491543	H	1.197211	0.231379	-2.296075
H	-3.955368	-4.156766	-1.602461	H	0.614480	2.440463	3.204170

H	-5.296890	-5.111361	-0.739642	H	2.371781	2.469596	2.896297
H	-3.061535	0.182337	2.468857	H	1.709166	1.553309	4.282935
H	-4.167149	1.350225	3.233422	H	6.017102	-2.390180	-0.185498
H	-2.712901	1.922286	2.369860	H	5.297188	-1.971676	-1.745164
H	-1.836937	0.655736	-4.024574	H	6.926138	-1.356596	-1.334268
H	-2.981325	-0.578140	-3.461555	H	3.224521	-2.187393	1.576822
H	-3.390932	1.148774	-3.295328	H	2.808502	-2.106348	3.281925
H	-0.926819	5.118520	1.712842	H	-4.646783	-3.547713	-1.506582
H	-1.918098	6.498155	1.146195	H	-3.277349	-4.507292	-0.911300
H	-2.632946	5.206294	2.163445	H	-3.273386	-3.885650	-2.575906
2-1				2-2			
C	-4.546769	-1.696945	-0.213130	C	0.105831	2.587464	-0.865062
C	-4.931630	-1.091616	1.157159	C	-0.822777	3.146260	0.238888
O	-6.127597	-1.876910	1.582965	O	-0.416978	4.583535	0.352113
C	-6.057439	-3.153306	1.003555	C	0.931731	4.696987	-0.011435
C	-4.969547	-3.138009	-0.028755	C	1.360370	3.401489	-0.631744
C	-3.080722	-1.443987	-0.574801	C	0.229161	1.058613	-0.815552
C	-2.777670	0.014459	-0.829385	C	-1.065364	0.360739	-1.169041
C	-3.185743	1.123004	-0.187631	C	-2.318831	0.580275	-0.730059
C	-4.079333	1.331307	1.022902	C	-2.934100	1.687518	0.120766
C	-5.300285	0.381673	1.132297	C	-2.305899	3.091622	-0.083126
C	-1.894206	0.369176	-2.027418	C	-1.081128	-0.661091	-2.312105
C	-1.421595	1.814820	-1.720187	C	-2.397574	-1.461903	-2.109614
C	-2.578831	2.358743	-0.847433	C	-3.279787	-0.424990	-1.353885
O	-0.826910	-0.660526	-2.123660	O	0.142847	-1.490166	-2.396409
C	0.534237	-0.424053	-2.006987	C	0.330819	-2.611861	-1.632227

C	0.961349	1.031644	-1.782730	C	-0.802046	-3.029445	-0.704807
C	-0.099575	1.766837	-0.941457	C	-0.579343	-2.339058	0.657469
C	2.369347	1.057522	-1.212335	C	-1.624387	-2.010894	1.520463
C	3.463115	0.993402	-2.081259	C	-1.344844	-1.312935	2.693571
C	4.751814	0.912625	-1.571491	C	-0.047770	-0.905637	3.023346
C	4.999115	0.908753	-0.191996	C	1.028145	-1.323436	2.208952
C	3.910422	0.986236	0.701342	C	0.734078	-2.056583	1.057533
C	2.612734	1.063079	0.163371	C	0.108466	0.177128	4.069844
C	6.475945	0.767385	0.192501	C	5.926145	0.816205	-2.006305
C	4.191038	-2.837915	-1.689724	C	3.423947	-0.902431	1.309599
C	4.468995	-0.541745	2.650825	C	2.479495	-0.945576	2.548050
C	4.041050	0.897643	2.226571	C	4.780767	-0.086116	-1.600773
C	4.620061	-2.682456	-0.256002	C	5.278588	-1.234568	-1.046050
O	3.644530	-3.160064	0.575265	O	4.311109	-2.306912	-0.658548
C	3.805264	-2.980412	2.047736	C	4.028566	-2.262317	0.849467
C	3.322994	-1.576660	2.471433	C	0.035028	1.511394	3.422738
O	7.182832	-0.078467	-0.756191	O	3.029543	-1.864360	3.671086
C	5.677912	-2.193489	0.164807	C	3.576679	0.161846	-1.718200
O	-4.553999	-4.253118	-0.620518	O	2.635109	3.141185	-0.906618
C	-6.787994	-4.069698	1.335134	C	1.584860	5.708783	0.180940
O	-3.200609	1.300248	2.306743	O	-3.003172	1.327697	1.630170
C	1.287647	-1.379969	-2.113911	C	1.411279	-3.196877	-1.690335
O	-2.669044	0.264411	-3.349731	O	-1.062695	0.085271	-3.658642
C	-2.022914	3.315222	0.149337	C	-4.127737	-1.091325	-0.316782
O	-2.787247	4.451390	0.419693	O	-5.460479	-0.676429	-0.243105
C	-1.999611	5.378442	1.314219	C	-6.191138	-1.528774	0.767620

C	-3.923590	4.606174	-0.010665	C	-5.909366	0.252500	-0.902165
O	4.957548	1.988080	2.835793	O	-2.179793	-2.821839	-1.384598
H	-5.195973	-1.241286	-0.975215	H	-0.316569	2.887806	-1.835502
H	-4.136616	-1.295345	1.882859	H	-0.597927	2.672827	1.201021
H	-2.801080	-2.013493	-1.466833	H	1.023087	0.704194	-1.482400
H	-2.440741	-1.817127	0.236955	H	0.520458	0.757720	0.199164
H	-4.488409	2.345082	0.929934	H	-3.973286	1.768586	-0.226864
H	-5.989048	0.559041	0.298291	H	-2.824294	3.795368	0.578012
H	-5.834747	0.615383	2.060426	H	-2.456431	3.428847	-1.115555
H	-1.294972	2.397823	-2.638265	H	-2.848177	-1.666180	-3.085236
H	-3.332208	2.907500	-1.420411	H	-3.981162	0.073013	-2.029434
H	0.988259	1.501208	-2.778726	H	-0.659088	-4.105931	-0.550359
H	0.237053	2.779994	-0.716634	H	-2.653379	-2.187284	1.241811
H	-0.263455	1.248232	0.007932	H	-2.164537	-1.003496	3.332347
H	3.299905	0.976865	-3.153933	H	1.538011	-2.375618	0.415348
H	5.609357	0.799591	-2.222798	H	1.032863	0.073577	4.646885
H	1.777008	1.106473	0.853580	H	-0.734875	0.164253	4.761854
H	6.958948	1.749167	0.139239	H	5.543672	1.673845	-2.558797
H	6.579162	0.396066	1.215231	H	6.452926	1.156670	-1.108228
H	4.986323	-2.498169	-2.352563	H	6.638205	0.253028	-2.614737
H	3.951953	-3.887639	-1.886349	H	2.892595	-0.443223	0.471864
H	3.277433	-2.253357	-1.853232	H	4.260314	-0.235450	1.552457
H	5.317446	-0.863192	2.046650	H	2.460493	0.079131	2.944633
H	4.785726	-0.525200	3.701696	H	4.821633	-3.231955	-0.933300
H	3.035892	1.068371	2.637788	H	3.396382	-2.200108	-1.243620
H	3.171620	-3.768218	2.456073	H	3.349667	-3.094588	1.064647

H	4.849825	-3.151576	2.319362	H	4.957487	-2.457832	1.396296
H	2.748716	-1.657152	3.402159	H	0.828092	1.577747	2.824503
H	2.635696	-1.241708	1.687017	H	2.406977	-1.791208	4.568635
H	6.790254	-0.992807	-0.603617	H	4.054996	-1.578811	3.933065
H	-3.770694	-4.263959	-1.370380	H	3.027154	-2.908229	3.344246
H	-5.008214	-5.201544	-0.348889	H	2.964173	2.203634	-1.342305
H	-2.753592	0.312408	2.452537	H	3.381111	3.895824	-0.668735
H	-3.803107	1.548030	3.188076	H	-3.596011	2.088862	2.152130
H	-2.394555	2.030213	2.201725	H	-3.493992	0.359018	1.747270
H	-2.000748	0.478744	-4.190118	H	-2.016339	1.277144	2.096387
H	-3.064315	-0.747472	-3.473791	H	-0.169483	0.713059	-3.722010
H	-3.499640	0.976846	-3.355805	H	-1.953237	0.713024	-3.748925
H	-1.026228	5.588068	0.862513	H	-1.035109	-0.640010	-4.477652
H	-2.559522	6.300815	1.465025	H	-6.075687	-2.586012	0.513253
H	-1.820946	4.889292	2.277553	H	-5.752588	-1.372201	1.758667
H	4.892598	1.958010	3.930054	H	-7.244816	-1.251941	0.781157
H	4.644109	2.981119	2.496584	H	-2.987955	-2.969954	-0.668999
H	6.003143	1.842791	2.554625	H	-2.269875	-3.613331	-2.137289

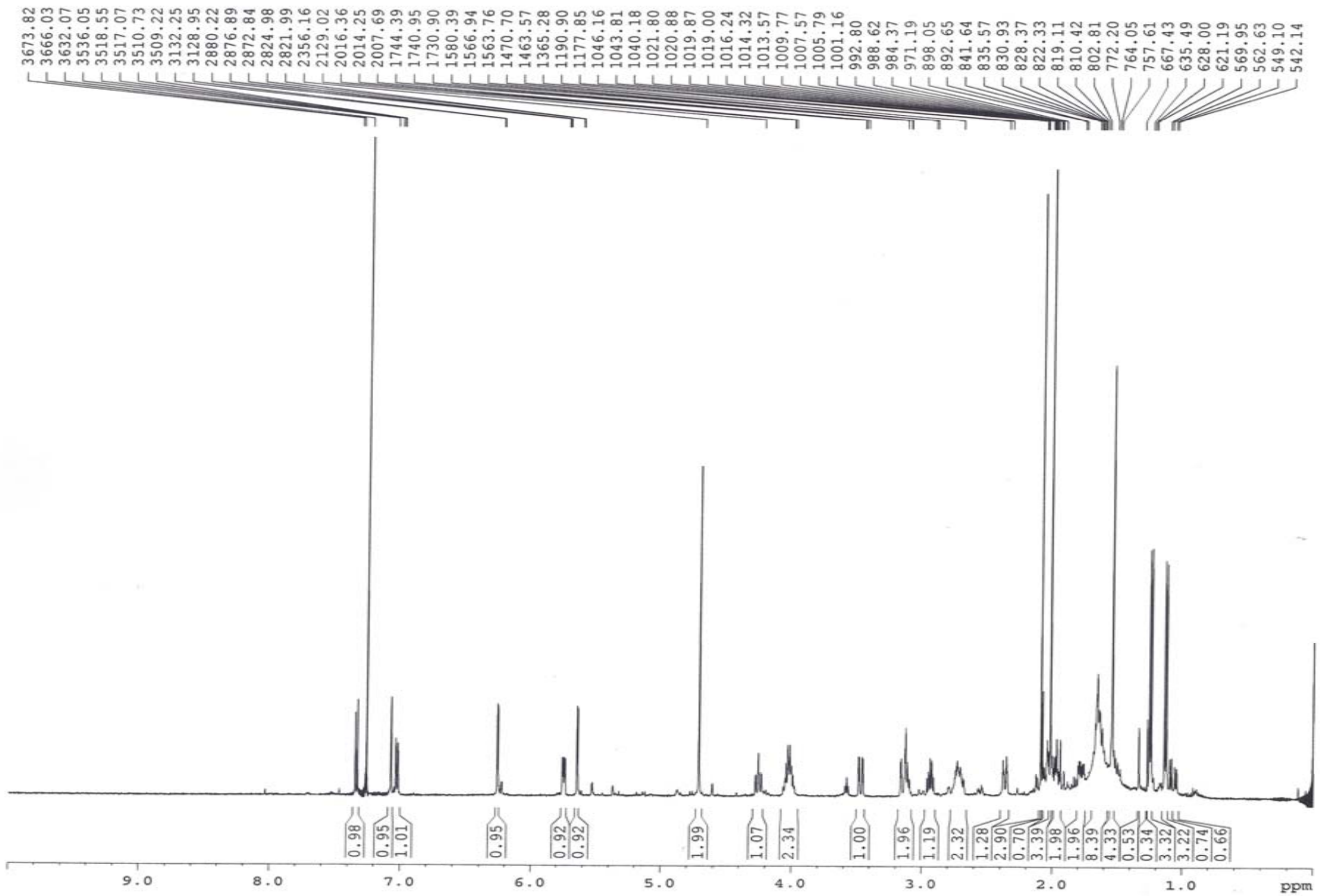
Table S4 ^{1}H NMR spectroscopic data for compounds **2–5** in $CDCl_3$ (500 MHz, *J* in Hz within parentheses)

No.	**2**	**3**	**4**	**5**
1	3.60 (1H, m); 3.36 (1H, m)	3.58 (1H, m); 3.35 (1H, m)	3.59 (1H, m); 3.36 (1H, m)	3.59 (1H, m); 3.36 (1H, m)
2	1.31 (2H, m)	1.29 (2H, m)	1.37 (2H, m)	1.37 (2H, m)
3	1.26 (2H, m)	1.26 (2H, m)	1.27 (2H, m)	1.27 (2H, m)
4	2.66 (1H, m)	2.66 (1H, m)	2.67 (1H, m)	2.67 (1H, m)
6	5.59 (1H, s)	5.56 (1H, s)	5.57 (1H, s)	5.57 (1H, s)
7	2.54 (1H, m)	2.53 (1H, m)	2.55 (1H, m)	2.55 (1H, m)
8	5.01 (1H, m)	5.03 (1H, m)	5.03 (1H, brs)	5.03 (1H, brs)
9	2.71 (1H, m); 2.36 (1H, m)	2.66 (1H, m); 2.34 (1H, m)	2.67 (1H, m); 2.36 (1H, m)	2.67 (1H, m); 2.36 (1H, m)
13	2.57 (1H,d,J=3.2); 2.08 (1H, m)	2.55 (1H, m); 2.06 (1H, m)	2.55 (1H, m); 2.08 (1H, m)	2.55 (1H, m); 2.08 (1H, m)
14	1.80 (3H, s)	1.80 (3H, s)	1.80 (3H, s)	1.80 (3H, s)
15	0.90 (3H,d,J=7.0)	0.88 (3H,d,J=7.0)	0.91 (3H,d,J=7.0)	0.91 (3H,d,J=7.0)
2'	4.56 (1H, s)	4.56 (1H, s)	4.56 (1H, s)	4.56 (1H, s)
3'	2.79 (1H, m)	2.80 (1H, m)	2.79 (1H, m)	2.79 (1H, m)
6'	2.97 (1H,d,J=15.9);	2.97 (1H,d,J=16.0)	2.96 (1H,d,J=16.0)	2.96 (1H,d,J=16.0)
	2.08 (1H, m)	2.06 (1H, m)	2.10 (1H, m)	2.10 (1H, m)
7'	2.73 (1H, m)	2.77 (1H, m)	2.79 (1H, m)	2.79 (1H, m)
8'	4.18 (1H,ddd,J=11.5,8.5,3.0)	4.18 (1H,ddd,J=12.0,9.0,3.5)	4.18 (1H,ddd,J=12.0,8.5,3.0)	4.18 (1H,ddd,J=11.5,8.5,3.0)
9'	2.39 (1H, m); 2.08 (1H, m)	2.37 (1H, m); 2.02 (1H, m)	2.36 (1H, m); 2.04 (1H, m)	2.36 (1H, m); 2.04 (1H, m)
10'	2.25 (1H, m)	2.26 (1H, m)	2.26 (1H, m)	2.26 (1H, m)
13'	6.21 (1H,d,J=3.3)	6.20 (1H,d,J=3.3)	6.20 (1H,d,J=3.2)	6.20 (1H,d,J=3.2)
	5.51 (1H,d,J=3.0)	5.51 (1H,d,J=3.0)	5.51 (1H,d,J=2.9)	5.51 (1H,d,J=2.9)
14'	1.03 (3H,d,J=7.3)	1.03 (3H,d,J=7.2)	1.03 (3H,d,J=7.2)	1.03 (3H,d,J=7.2)
15'	1.63 (3H,d,J=1.0)	1.63 (3H,d,J=1.1)	1.63 (3H, s)	1.63 (3H, s)
2''	2.03 (3H, s)	2.04 (3H, s)	2.08 (3H, s)	2.08 (3H, s)
2'''	1.98 (3H, s)	2.44 (1H, m)	2.26 (1H, m)	2.10 (2H, m)
3'''		1.11 (3H,d,J=7.0)	1.68 (1H, m); 1.37 (1H, m)	2.08 (1H, m)
4'''		1.11 (3H,d,J=7.0)	0.92 (3H,t,J=6.5Hz)	0.93 (3H,d,J=6.5)
5'''			1.09 (3H,d,J=7.0)	0.93 (3H,d,J=6.5)

Table S5. ^{13}C NMR spectroscopic data for compounds **2-5** in $CDCl_3$ (125 MHz)

No.	**2**	**3**	**4**	**5**
1	62.7 t	62.7 t	62.6 t	62.7 t
2	31.0 t	31.0 t	31.0 t	31.0 t
3	32.3 t	32.3 t	32.3 t	32.4 t
4	34.6 d	34.4 d	34.4 d	34.5 d
5	132.4 s	132.7 s	132.7 s	132.6 s
6	66.0 d	65.8 d	65.8 d	65.8 d
7	49.7 d	49.4 d	49.2 d	49.5 d
8	76.2 d	76.1 d	76.0 d	76.2 d
9	34.5 t	34.7 t	34.6 t	34.7 t
10	134.1 s	134.2 s	134.3 s	134.2 s
11	55.7 s	55.6 s	55.5 s	55.6 s
12	178.5 s	178.5 s	178.4 s	178.5 s
13	34.9 t	34.7 t	34.8 t	34.8 t
14	20.9 q	20.9 q	20.8 q	20.9 q
15	19.1 q	19.2 q	19.2 q	19.2 q
1'	63.1 s	63.1 s	63.1 s	63.1 s
2'	81.3 d	81.2 d	81.1 d	81.2 d
3'	57.6 d	57.8 d	57.8 d	57.8 d
4'	134.1 s	134.2 s	134.2 s	134.2 s
5'	137.2 s	137.1 s	136.9 s	137.1 s
6'	26.2 t	26.1 t	26.1 t	26.1 t
7'	45.1 d	45.0 d	44.8 t	45.0 t
8'	82.5 d	82.5 d	82.5 d	82.5 d
9'	36.1 t	36.0 t	35.9 t	36.0 t
10'	29.7 d	29.7 d	29.6 d	29.6 d
11'	139.5 s	139.5 s	139.5 s	139.5 s
12'	170.1 s	170.1 s	170.1 s	170.1 s
13'	119.3 t	119.3 t	119.2 t	119.3 t
14'	17.0 q	17.0 q	16.9 q	17.0 q
15'	14.3 q	14.3 q	14.2 q	14.3 q
1''	170.6 s	170.8 s	170.8 s	170.8 s
2''	20.9 q	21.0 q	21.0 q	20.9 q
1'''	169.7 s	175.6 s	175.2 s	171.8 s
2'''	21.4 q	34.1 d	41.0 d	43.8 t
3'''		18.8 q	26.1 t	25.4 d
4'''		18.7 q	11.6 q	25.5 t
5'''			16.3 q	25.6 t

Fig. 8S. ^{1}H NMR spectrum of neojaponicone A (**1**) in $CDCl_3$.



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EXPNO 1
PROCNO 1

F2 - Acquisition Parameters
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Time 16.58
INSTRUM spect
PROBHD 5 mm Multinucl
PULPROG zg30
TD 32768
SOLVENT CDCl3
NS 16
DS 2
SWH 15015.015 Hz
FIDRES 0.458222 Hz
AQ 1.0912577 sec
RG 64
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DE 6.50 usec
TE 300.0 K
D1 2.00000000 sec
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SFO1 500.1320088 MHz

F2 - Processing parameters
SI 32768
SF 500.1300140 MHz
WDW no
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LB 0.00 Hz
GB 0
PC 1.00

Fig. 9S. ^{13}C NMR spectrum of neojaponicone A (**1**) in $CDCl_3$.

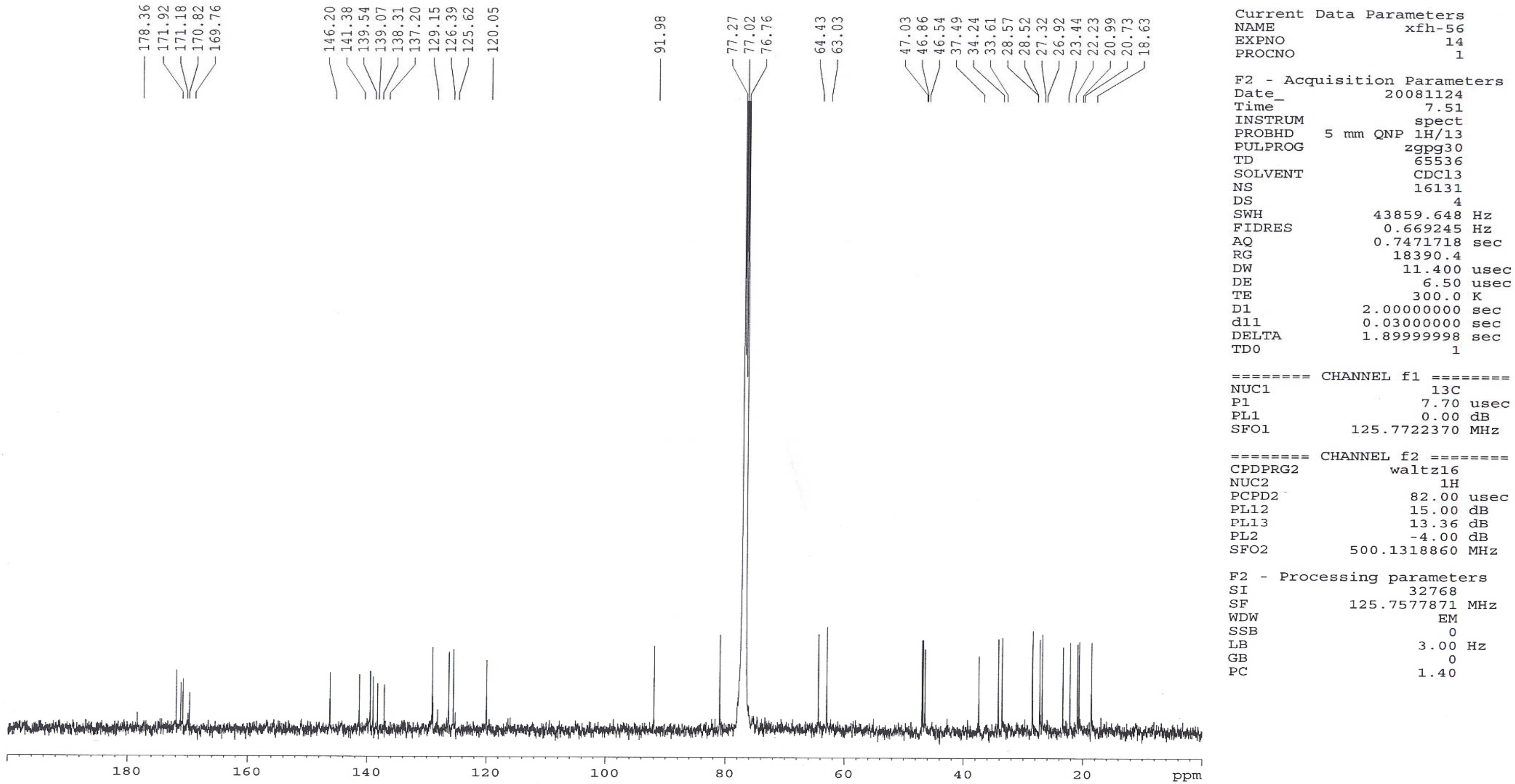

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Fig. 10S. DEPT NMR spectrum of neojaponicone A (**1**) in $CDCl_3$.

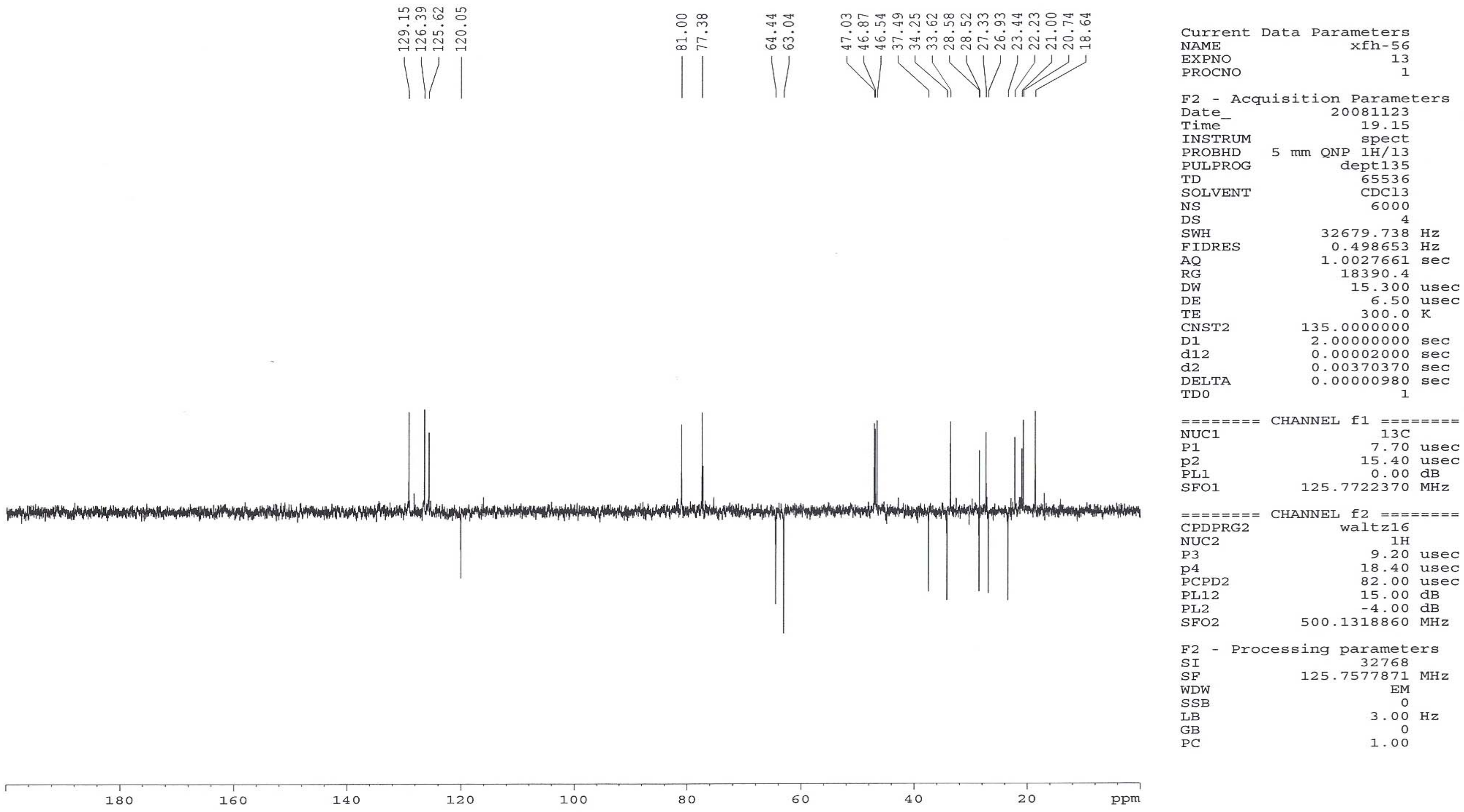

Fig. 11S. HSQC NMR spectrum of neojaponicone A (**1**) in $CDCl_3$.

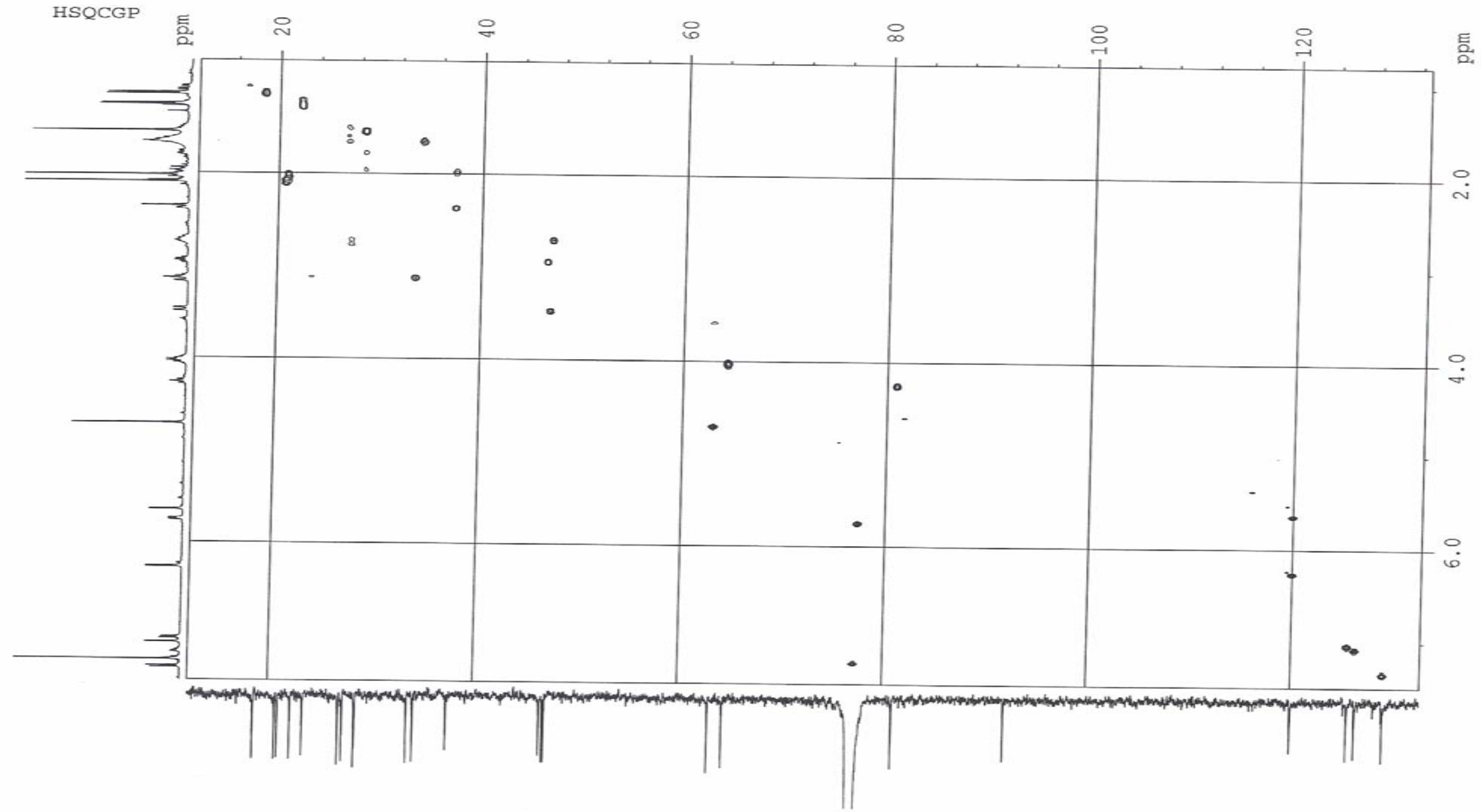

Fig. 12S. ^{1}H-^{1}H COSY NMR spectrum of neojaponicone A (**1**) in $CDCl_3$.

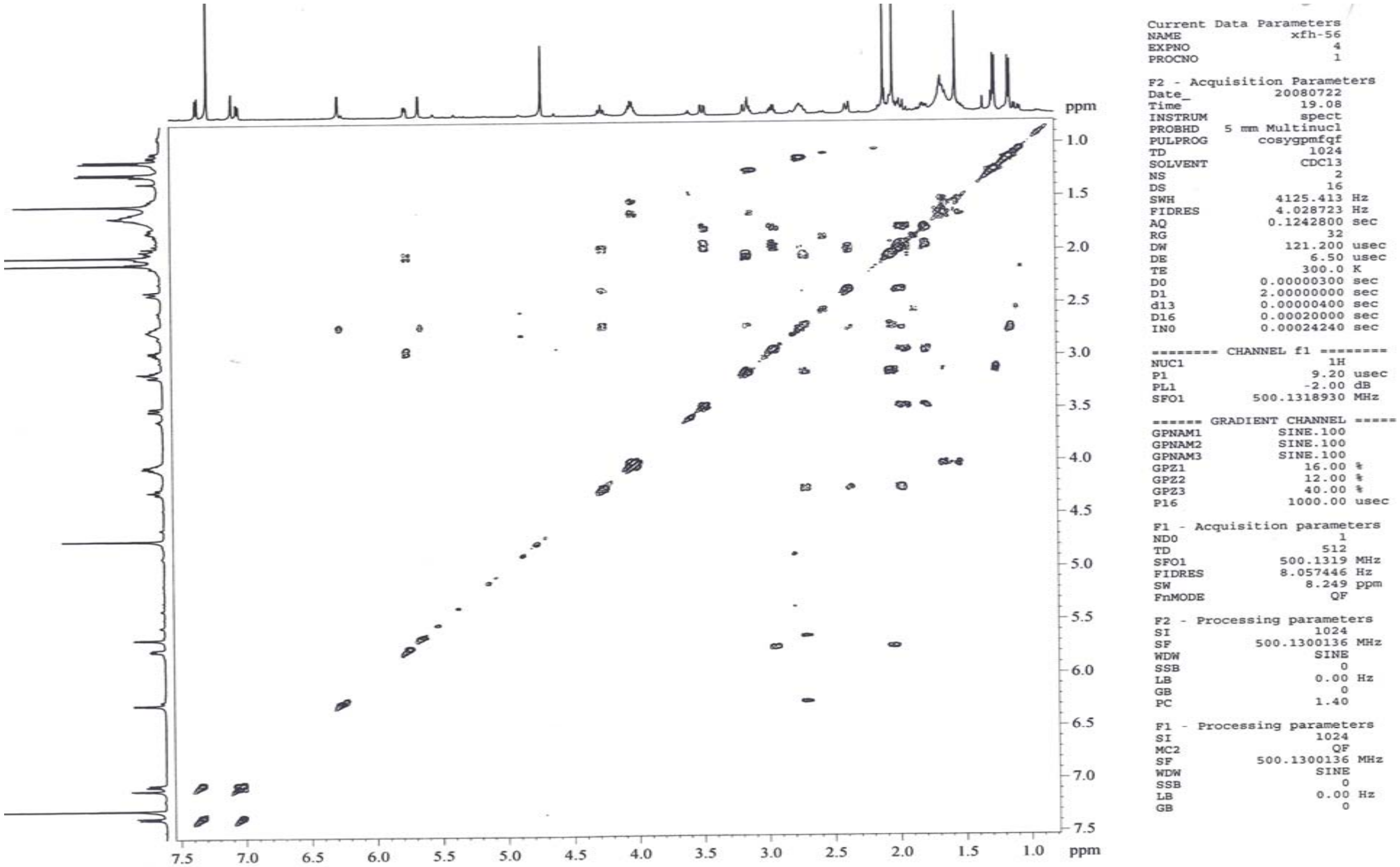

Fig. 13S. HMBC NMR spectrum of neojaponicone A (**1**) in $CDCl_3$.

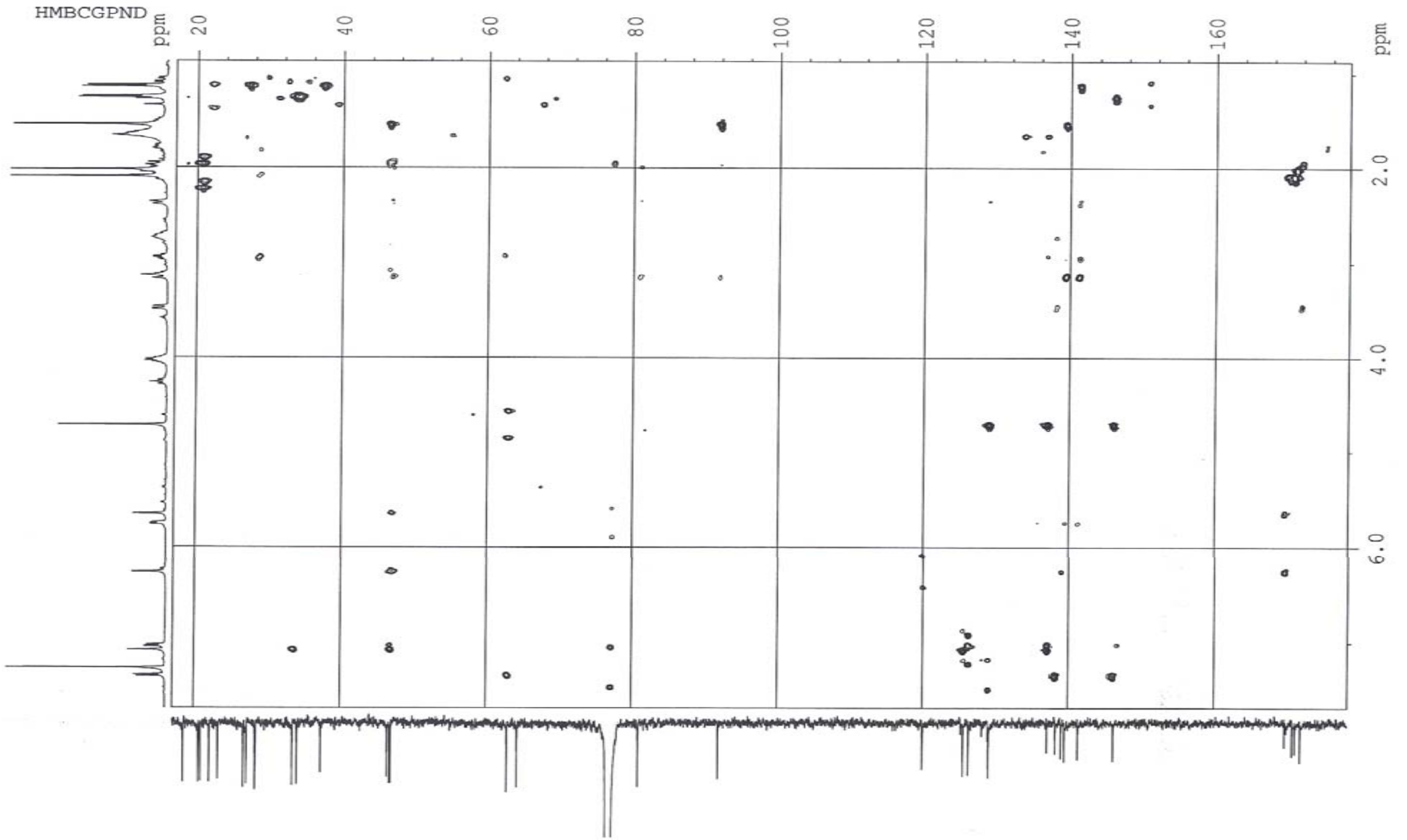

Fig. 14S. NOESY NMR spectrum of neojaponicone A (**1**) in $CDCl_3$.

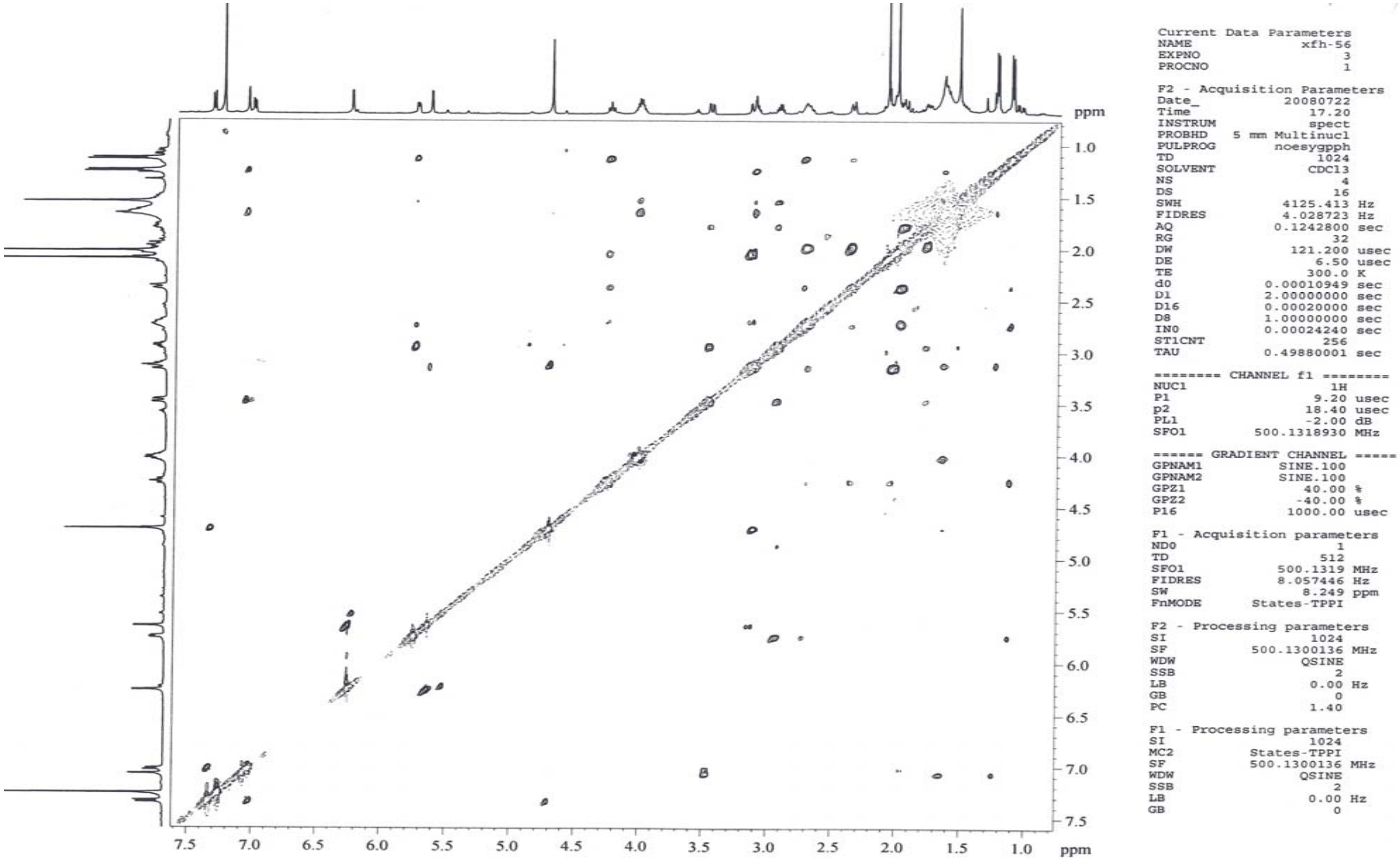

Fig. S15. ^{1}H NMR spectrum of japonicone M (**2**) in $CDCl_3$.

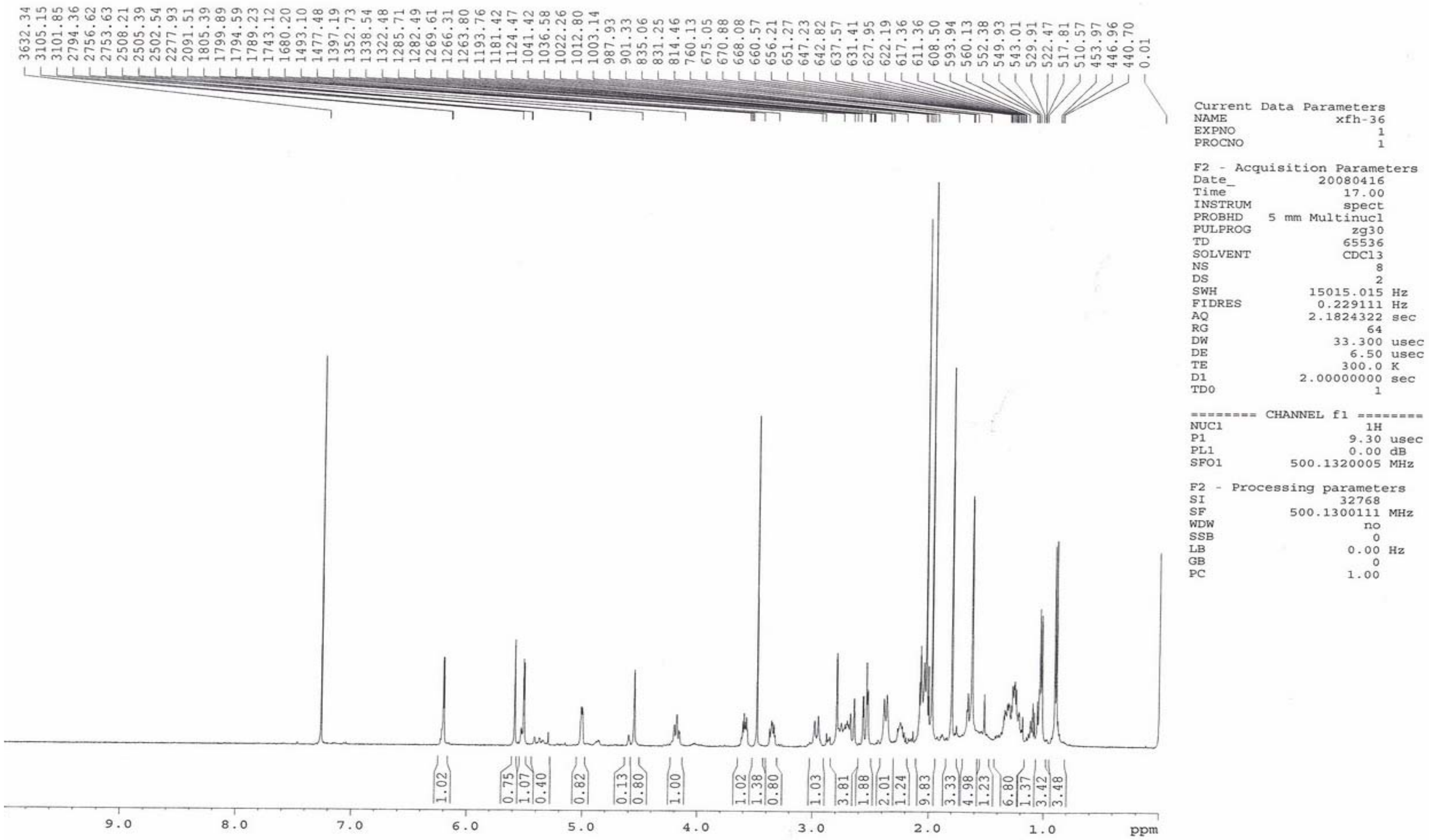

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Fig. S16. ^{13}C NMR spectrum of japonicone M (**2**) in $CDCl_3$.

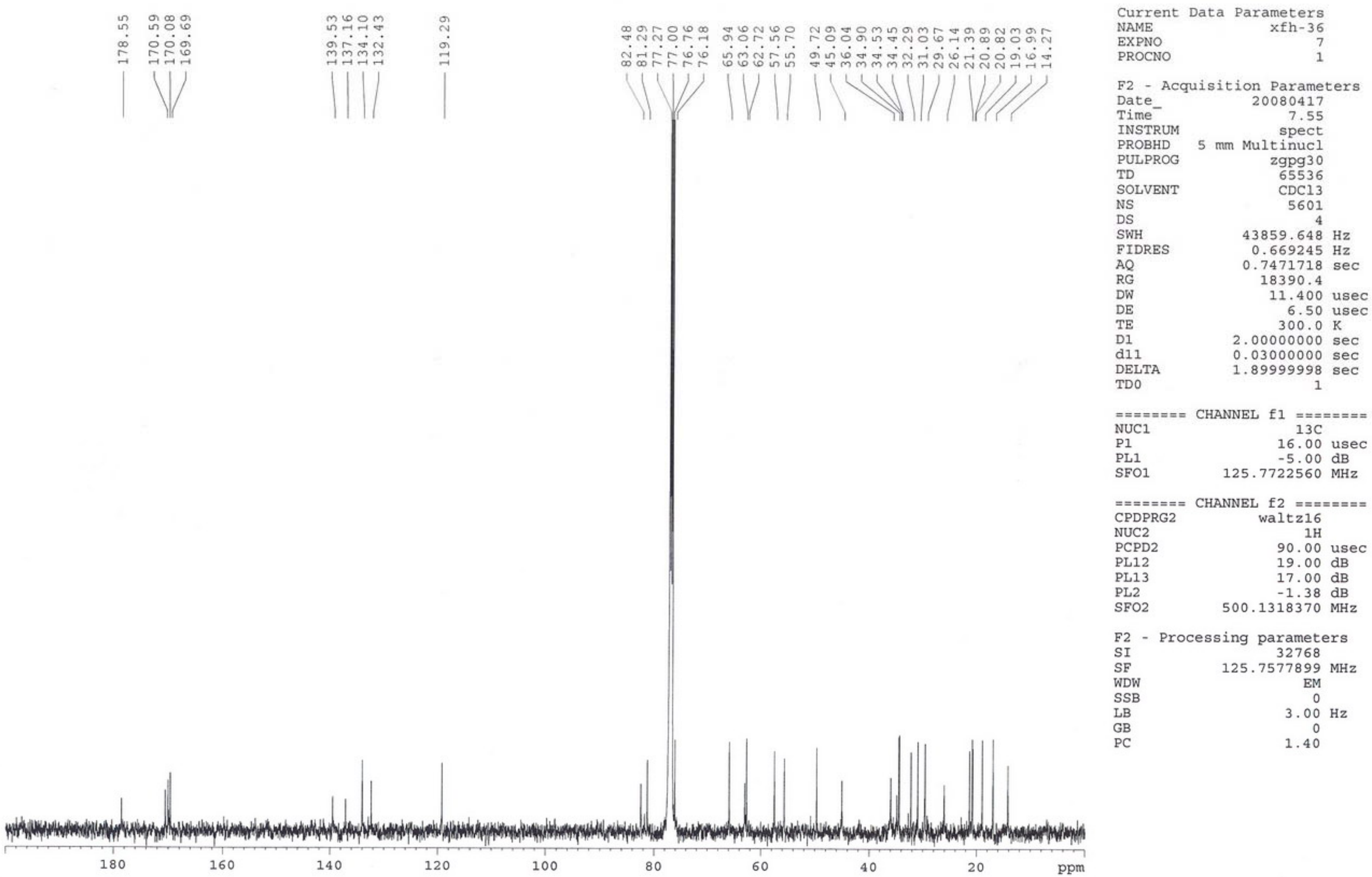

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Fig. S17. DEPT NMR spectrum of japonicone M (**2**) in $CDCl_3$.

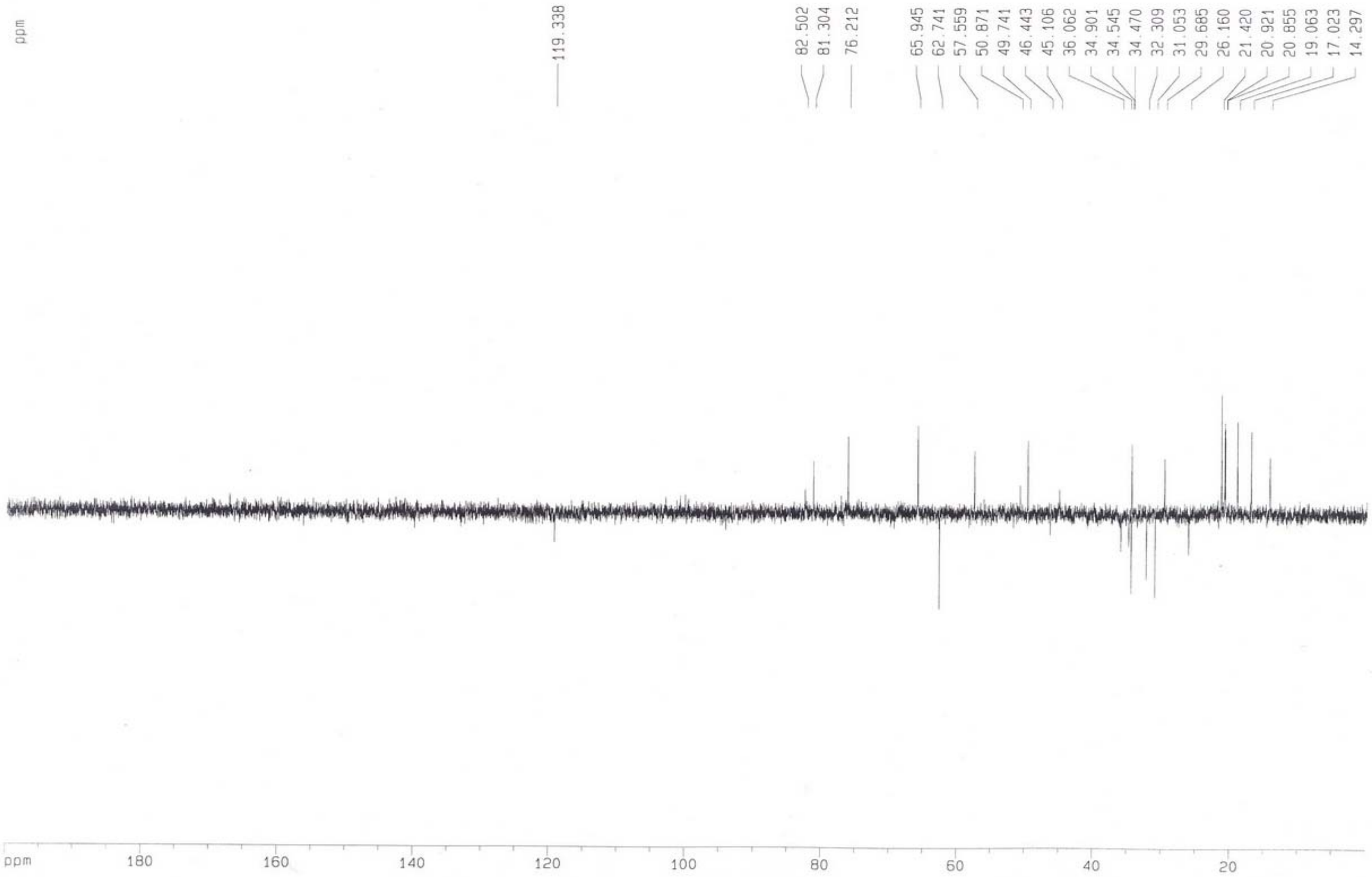

Fig.S18. HSQC NMR spectrum of japonicone M (**2**) in $CDCl_3$.

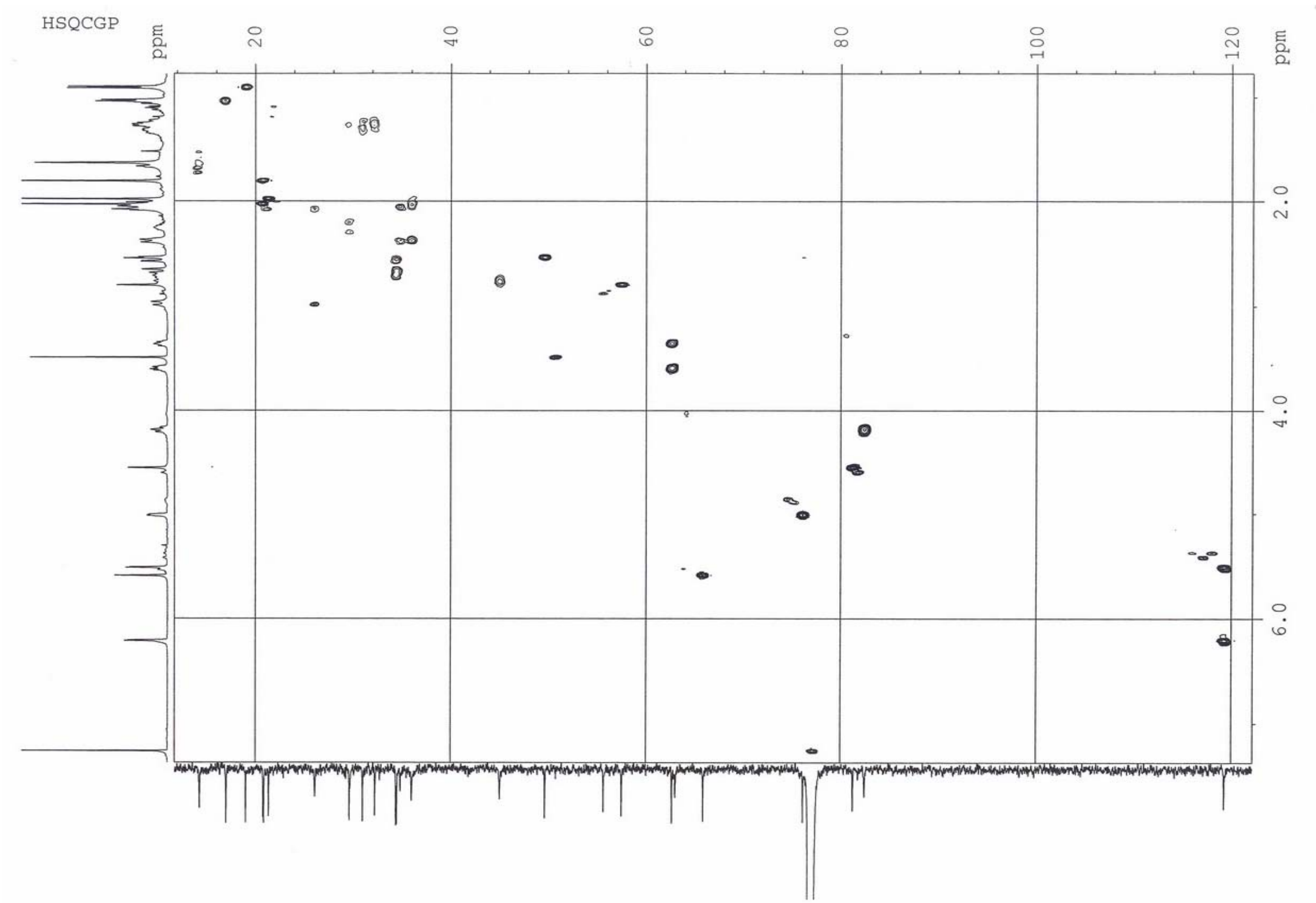

Fig. S19. ^{1}H-^{1}H COSY NMR spectrum of japonicone M (**2**) in $CDCl_3$.

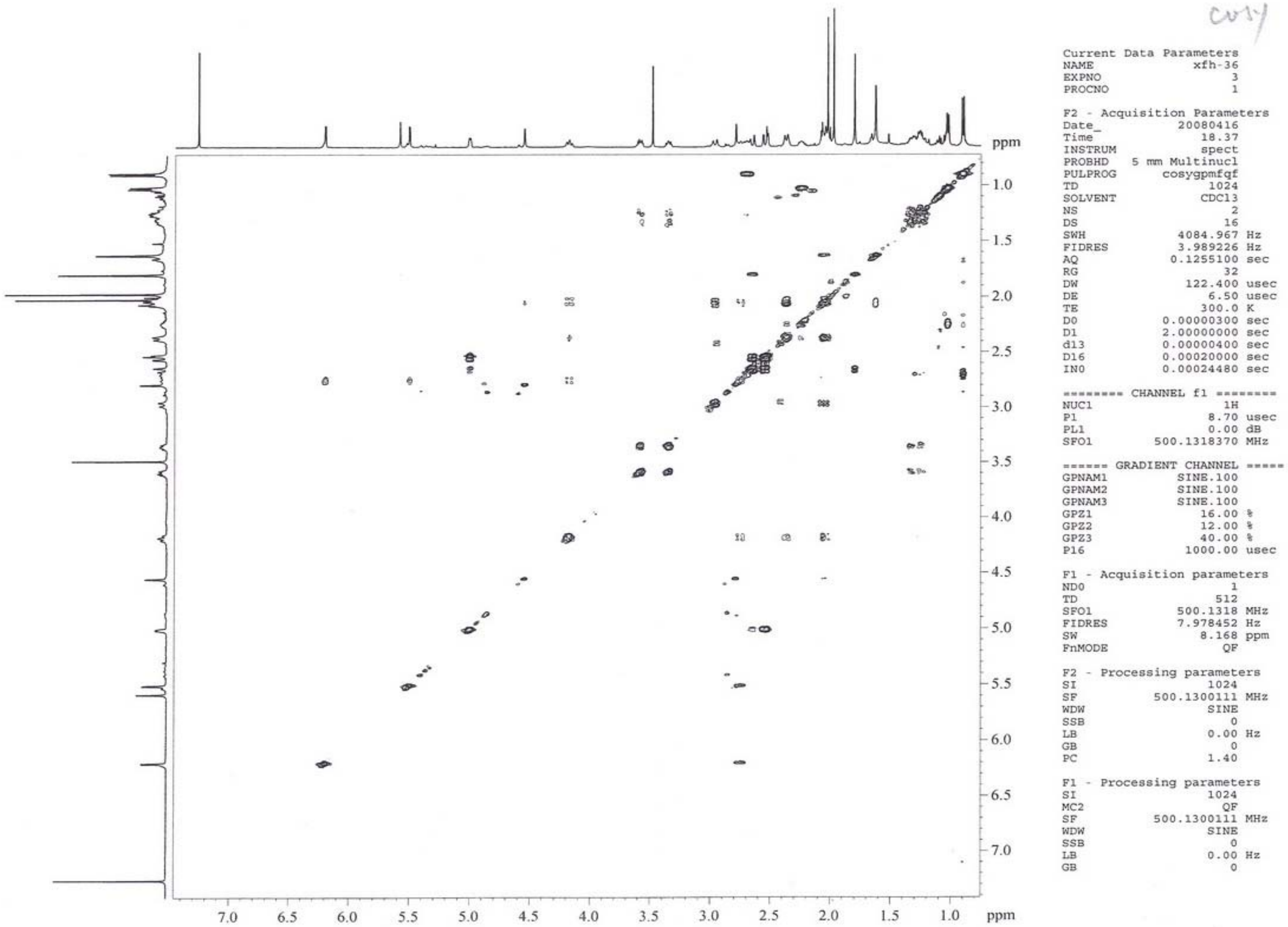

Fig. S20. HMBC NMR spectrum of japonicone M (**2**) (**1**) in $CDCl_3$.

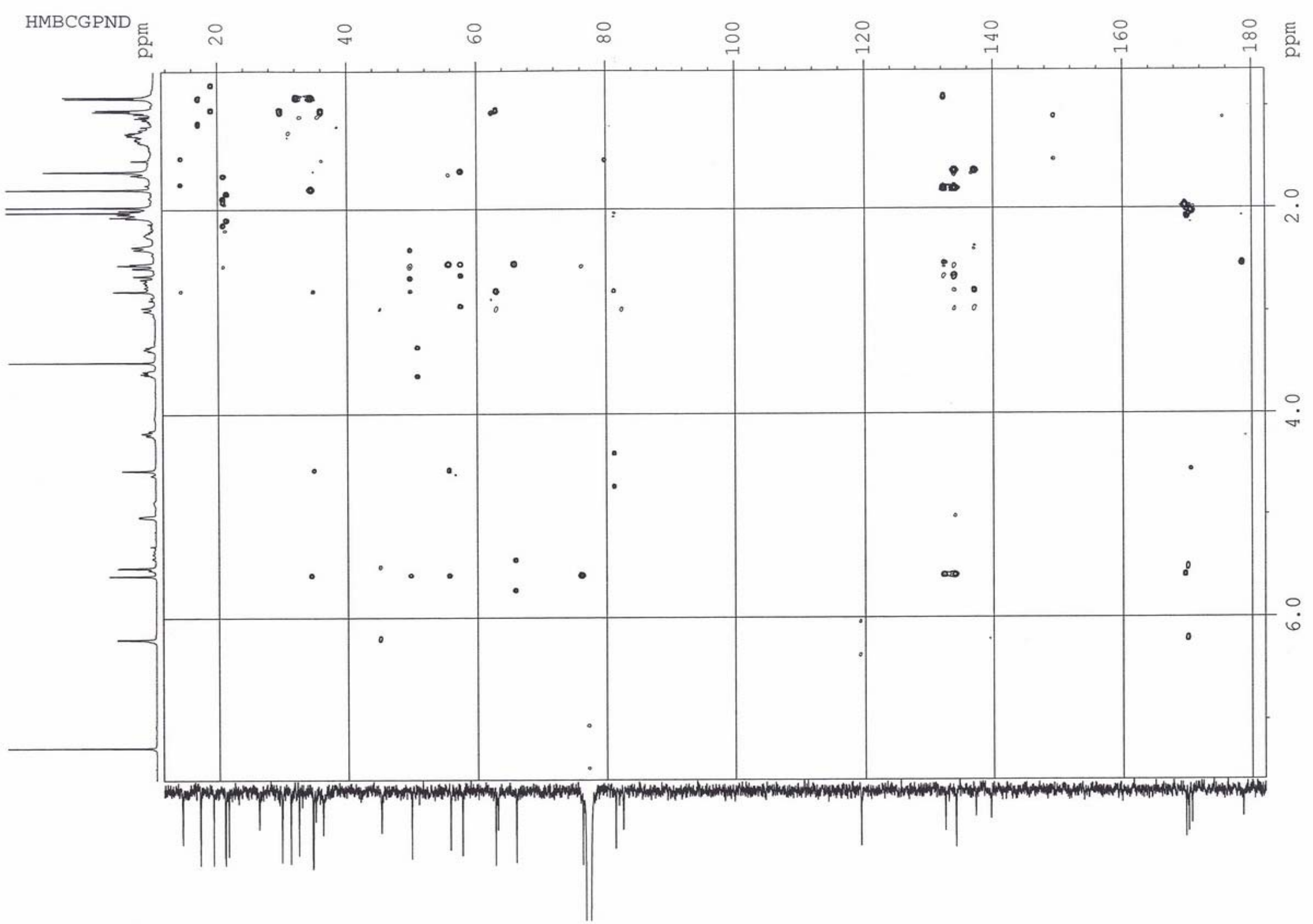

Fig. S21. NOESY NMR spectrum of japonicone M (**2**) (**1**) in $CDCl_3$.