Electronic Supplementary Material (ESI) for Chemical Communications.

Supporting Information

Enhancing the Utility of $^{1}J_{CH}$ Couplings Constants in Structural Studies Through Optimized DFT Analysis

Alexei V. Buevich, Josep Saurí, Teodor Parella, Nunziatina De Tommasi, Giuseppe Bifulco, R. Thomas Williamson, and Gary E. Martin*

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Computational Methods

Force field calculations were done using Spartan '16[1] and PCModel V.10[2] software programs on a Windows7 PC equipped with an i5 Intel CPU@ 2.3 GHz, 8 GB RAM. Principal component analysis (PCA) was done using SIMCA-P v.10 program.[3] All QM calculations were done using Gaussian16 software package.[4] QM calculations were carried out either on Cray XC30 supercomputer or Linux cluster. From 12 to 16 processors and 25 GB of RAM were usually utilized for each calculation. Up to 80 simultaneous calculations were run depending of the available computational resources at the time. All basis sets for QM calculations were either standard ones from Gaussian16 or were downloaded from EMSL basis set exchange portal.[5] Computational time that was required for *J*-coupling calculations was dependent of the type of functional, basis set, method of calculation (mixed[6] vs spinspin) and the platform that was used for the calculation. The mixed algorithm was somewhat slower than spinspin, however in general the "mixed" results were of higher accuracy (see PCA analysis below) and the computational time for the most optimal combination of functional and basis set B3LYP/6-31G(d,p) for $^1J_{CH}$ coupling calculations was still shorter than those of the majority of calculations that were performed using specialized basis sets for *J*-coupling calculations even with the spinspin algorithm. Here are examples of wall-clock times of *J*-coupling calculations for strychnine ($C_{21}H_{22}N_2O_2$, total number of *J*-couplings 1081) on Linux cluster (each calculation used up to 16 processors and 25 GB of RAM):

B3LYP/6-31G(d,p)	1.8 h (spinsspin)	2.0 h (mixed)
B3LYP/TZVP	5.5 h (spinspin)	10.5 h (mixed)
B3LYP/aug-cc-pVTZ-J	294 h (spinspin)	485 h (mixed)
pw91/aug-cc-pVTZ-J	20.2 h (spinspin)	36.5 h (mixed)
pbe/aug-cc-pVTZ-J	20.4 h (spinspin)	33.2 h (mixed)
B3LYP/6-31G-J	0.9 h (spinsspin)	
B3LYP/6-31+G(d)-J	5.2 h (spinsspin)	
B3LYP/6-311++G(d,p)-J	17.2 h (spinsspin)	
PBE/ccJ-pVDZ	23.0 h (spinspin)	
B3LYP/pcJ-0	0.5 h (spinsspin)	
B3LYP/pcJ-1	4.9 h (spinsspin)	
B3LYP/pcJ-2	80.7 h (spinsspin)	
B3LYP/epr-III	80.2 h (spinsspin)	

Root mean square deviations (RMSD), maximum *J*-coupling deviations (max_d), differences between mean values (ΔJ), and correlation coefficients (R) were used to compare calculated *J*-couplings with experimental. It is noteworthy, that in the process of comparison of the calculated with experimental *J*-couplings, no assignments of methylene protons were assumed. The assignments of the methylene protons would require utilization of additional spectroscopic data, such as proton-proton couplings, NOEs, chemical shifts. Herewith we relied only on the size of the $^1J_{CH}$ couplings, which is an unbiased, independent, and more challenging test compared with an analysis utilizing assigned protons. The only condition that we applied here was that for the pair of calculated couplings for methylene protons, we chose the assignment which provided the lowest RMSD. For example, if the set of two calculated couplings were 135 and 140 Hz and the experimental values were 141 and 134 Hz, we would correspondingly reverse assignments of the protons so the contributions to the RMSD value would be proportional to the (140-141) and (135-134) differences (total=2 Hz), instead of (141-135) and (140-134) (total=12 Hz). This procedure was done for each methylene pair in each trial structure.

Table 1S. RMSD and differences between mean values of experimental and calculated *J*-couplings (ΔJ) for 22 $^1J_{CH}$ couplings of strychnine.[a]

Method	Mixed RMSD, Hz	Mixed ΔJ, Hz[b]	Spinspin RMSD, Hz	Spinspin ΔJ, Hz[b]
B3LYP/6-31G	6.71	-6.40	23.73	-21.35
B3LYP/6-31G(d)	3.81	-3.41	12.56	-1.69
B3LYP/6-31+G(d)	4.43	-4.06	9.81	-2.73
B3LYP/6-31G(d,p)	3.24	-2.77	12.82	0.91
B3LYP/6-31+G(d,p)	3.91	-3.49	10.08	-0.78
B3LYP/6-311G(d,p)	5.34	-5.04	5.95	5.30
B3LYP/6-311+G(d,p)	5.74	-5.43	6.73	6.34
B3LYP/6-311++G(d,p)	5.73	-5.42	7.15	6.78
B3LYP/6-311++G(2d,p)	5.23	-4.92	8.11	7.71
B3LYP/6-31G(d,3pd)	3.41	-2.99	11.26	9.42
B3LYP/6-311G(2d,2p)	4.60	-4.27	12.26	11.89
B3LYP/6-311G(3d,2p)	4.84	-4.52	10.27	10.05
B3LYP/6-311G(2df,2pd)	4.70	-4.40	12.80	12.60
B3LYP/6-311G(2df,3pd)	4.84	-4.54	8.21	7.98
B3LYP/6-311G(3df,3pd)	4.78	-4.47	8.32	7.98
B3LYP/aug-cc-pVTZ	5.61	-5.34	14.67	13.99
B3LYP/aug-cc-pVTZ-J	8.58	-8.34	8.73	-8.50
pw91/aug-cc-pVTZ-J	4.35	3.98	4.13	3.71
pbe/aug-cc-pVTZ-J	5.45	5.18	5.46	5.18
B3LYP/6-31G-J	---[c]	---[c]	12.51	-12.32
B3LYP/6-31G-J//B3LYP/6-31G-J	---[c]	---[c]	13.41	-13.22
B3LYP/6-31+G(d)-J	---[c]	---[c]	10.47	-10.27
B3LYP/6-311++G(d,p)-J	---[c]	---[c]	10.19	-10.00
B3LYP/pcJ-0	7.87	7.30	11.51	10.98
B3LYP/pcJ-0//B3LYP/pcJ-0	---	---	10.48	9.00
B3LYP/pcJ-1	8.49	-8.21	7.46	-7.22
B3LYP/pcJ-1//B3LYP/pcJ-1	---	---	6.89	-6.65
B3LYP/pcJ-2	---[c]	---[c]	7.24	-7.01
B3LYP/pcJ-2_2006	---[c]	---[c]	9.34	-9.14
B3LYP/epr-III	7.29	-7.07	4.49	-4.16
B3LYP/epr-III//B3LYP/aug-cc-pVDZ	7.62	-7.37	4.82	-4.46
pbe/NMR-DKH	6.59	6.38	12.43	12.30
pbe/ccJ-pVDZ	---[c]	---[c]	7.00	6.77
B3LYP/TZVP	6.05	-5.75	3.19	2.27
B3LYP/TZVP//B3LYP/TZVP	---	---	3.69	3.03
B3PW91/6-311++G(d,p)// B3PW91/6-311++G(d,p)	5.95	5.73	17.09	16.92

[a] *J*-couplings were calculated in two approximations, mixed and spinspin (see text for details). Unless otherwise stated the geometry of strychnine was optimized at the B3LYP/6-31G(d) level; [b] $\Delta J = \overline{J^{exp}} - \overline{J^{calc}}$; [c] SFC convergence has failed

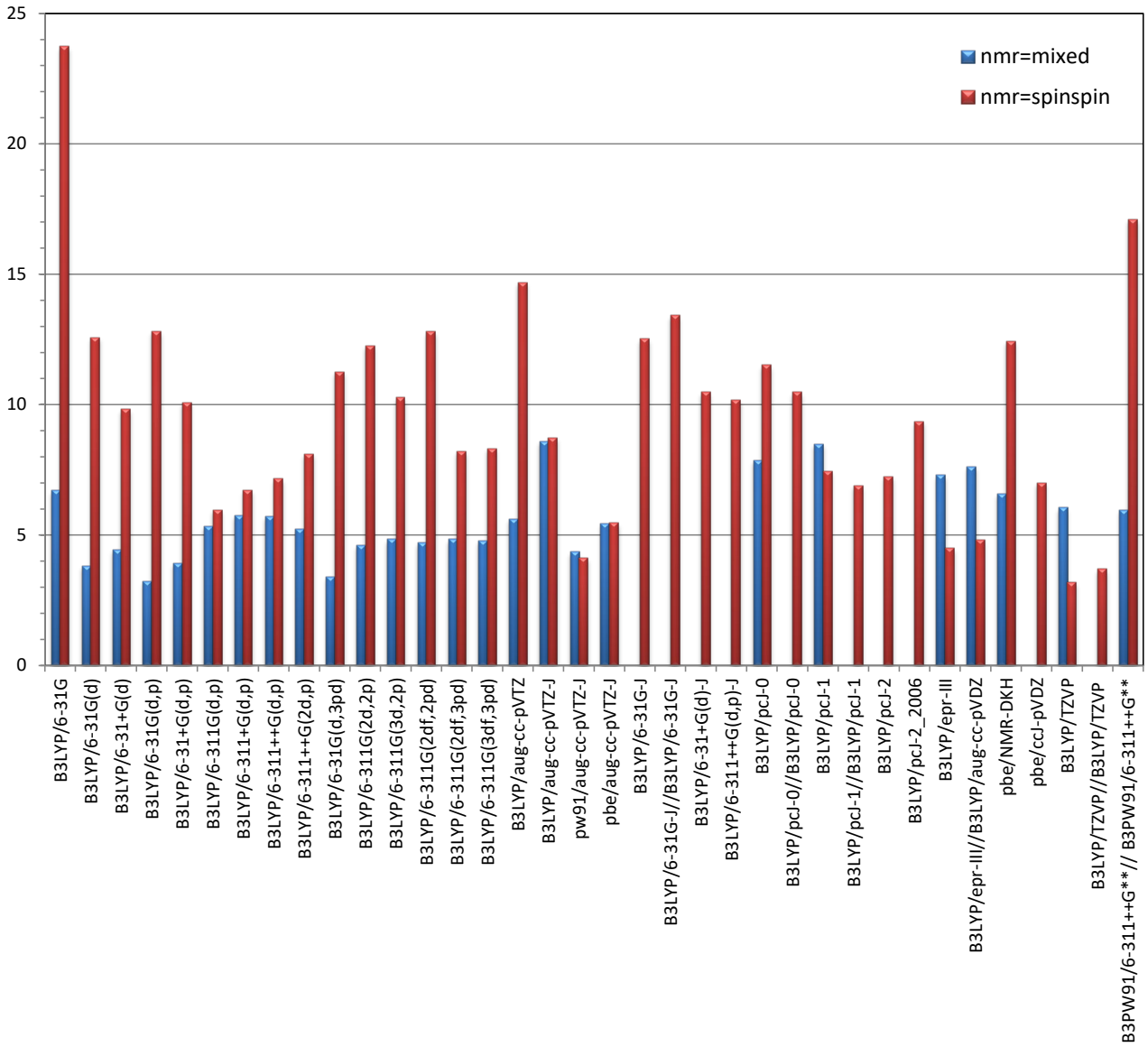
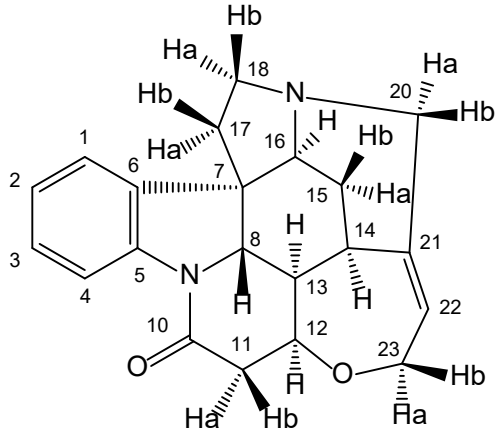


Figure 1S. RMSD of 22 $^{1}J_{CH}$ couplings of strychnine calculated in two approximations, mixed (blue) and spinspin (red), with 36 different methods. Unless otherwise stated the geometry of strychnine was optimized at the B3LYP/6-31G(d) level (see main text and Table 1S for more details).

Table 2S. $^{1}J_{CH}$ Couplings (Hz), RMSD and differences between mean values of experimental and calculated *J*-couplings (ΔJ) for 22 $^{1}J_{CH}$ couplings of strychnine.[a]



Protons	Exp.	b3lyp/6-31g		b3lyp/6-31g(d)		b3lyp/6-31+g(d)		b3lyp/6-31g(d,p)	
		mixed	spinspin	mixed	spinspin	mixed	spinspin	mixed	spinspin
H1	158.36	163.2	158.9	161.1	135.9	160.6	146.1	159.4	132.8
H11a	134.16	142.5	161.8	140.7	142.7	140.0	137.7	139.3	139.9
H11b	124.74	134.3	160.3	130.7	142.5	130.0	139.2	129.4	140.4
H12	149.12	152.0	171.6	150.3	152.5	150.0	151.4	148.7	150.1
H13	124.2	131.4	161.5	128.7	143.9	128.3	144.4	127.8	141.7
H14	129.82	136.0	160.6	133.9	141.5	133.5	139.8	132.9	138.4
H15a	130.96	136.3	155.6	133.9	138.5	133.3	136.5	133.1	136.0
H15b	129.94	135.9	158.6	133.7	141.1	133.1	136.5	132.7	139.1
H16	146.36	154.4	174.2	151.6	153.1	151.2	153.7	150.3	150.1
H17a/b	134.12	137.0	158.1	134.6	140.6	134.0	138.3	133.7	138.5
H17b/a	134.12	141.0	156.3	138.6	138.4	138.0	138.9	137.7	135.5
H18a	145.92	151.6	163.4	149.3	143.8	148.7	146.0	147.9	141.0
H18b	130.24	135.1	153.9	133.0	138.0	132.4	140.8	132.4	136.6
H2	159.8	167.1	162.2	165.0	138.5	164.4	143.7	163.2	135.4
H20a	138.16	144.7	166.7	142.2	149.8	141.5	145.6	140.8	148.0
H20b	137.86	143.0	161.1	141.0	142.7	140.4	140.4	139.9	139.7
H22	158.4	165.7	169.5	163.4	145.5	162.9	153.1	161.5	142.3
H23a	136.64	139.8	158.8	138.4	143.4	137.7	140.7	137.2	141.9
H23b	144.42	151.8	166.0	148.9	144.1	148.2	148.6	147.1	141.3
H3	158.6	165.7	161.6	163.7	138.0	163.2	143.5	161.8	135.0
H4	168.26	179.5	173.1	177.0	148.8	176.4	155.8	175.5	145.5
H8	144.94	152.2	175.1	148.7	153.2	148.4	158.5	147.9	150.2
RMSD, Hz		6.71	23.73	3.81	12.56	4.43	9.81	3.24	12.82
ΔJ, Hz		-6.40	-21.35	-3.41	-1.69	-4.06	-2.73	-2.77	0.91

Protons	Exp.	b3lyp/6-311g(2df,2pd)		b3lyp/6-311g(d,p)		b3lyp/6-311+g(d,p)		b3lyp/6-311++g(d,p)	
		mixed	spinspin	mixed	spinspin	mixed	spinspin	mixed	spinspin
H1	158.36	161.2	143.3	162.2	146.8	162.8	147.4	162.8	147.0
H11a	134.16	140.7	125.0	141.3	132.6	141.8	131.0	141.8	130.5
H11b	124.74	130.8	117.6	131.5	125.2	131.9	123.4	131.8	122.9
H12	149.12	150.9	131.6	151.2	141.4	151.9	140.4	151.9	139.9
H13	124.2	129.3	113.7	129.7	122.4	130.0	121.5	130.0	120.8
H14	129.82	134.5	117.0	135.0	126.2	135.3	125.3	135.3	124.9
H15a	130.96	134.3	119.2	134.9	126.7	135.1	125.3	135.0	125.1
H15b	129.94	134.2	119.1	134.7	126.8	134.9	125.2	134.9	124.9
H16	146.36	152.0	132.5	152.7	141.5	153.1	140.6	153.1	140.2
H17a/b	134.12	135.2	119.4	135.7	127.9	135.8	125.5	135.8	125.2
H17b/a	134.12	139.0	122.8	139.7	131.2	139.9	129.5	139.8	129.2
H18a	145.92	149.7	131.7	150.2	139.5	150.6	138.2	150.6	137.8
H18b	130.24	133.9	118.2	134.2	126.0	134.4	123.9	134.4	123.5
H2	159.8	165.1	147.0	166.1	151.1	166.9	151.1	166.8	150.4
H20a	138.16	142.2	125.0	142.8	134.2	143.2	132.1	143.2	131.8
H20b	137.86	141.5	125.1	142.0	132.6	142.2	130.3	142.2	130.2
H22	158.4	163.8	145.6	164.7	149.8	165.4	150.1	165.4	149.8
H23a	136.64	138.9	122.6	139.2	130.8	139.6	128.9	139.6	128.4
H23b	144.42	148.8	131.0	149.5	138.1	150.0	138.0	150.0	137.3
H3	158.6	163.7	146.0	164.7	149.8	165.6	149.9	165.5	149.2
H4	168.26	177.1	158.8	178.2	162.6	178.6	162.3	178.6	161.6
H8	144.94	149.2	129.6	149.8	139.4	150.0	139.8	150.0	139.2
RMSD, Hz		4.70	12.80	5.34	5.95	5.74	6.73	5.73	7.15
ΔJ, Hz		-4.40	12.60	-5.04	5.30	-5.43	6.34	-5.42	6.78

Protons	Exp.	b3lyp/6-311++g(2d,p)		b3lyp/6-31g(d,3pd)		b3lyp/6-31+g(d,p)		b3lyp/6-311g(3d,2p)	
		mixed	spinspin	mixed	spinspin	mixed	spinspin	mixed	spinspin
H1	158.36	162.2	146.2	159.6	137.5	160.6	143.1	161.7	144.4
H11a	134.16	141.4	129.9	139.5	127.7	140.0	135.6	140.8	126.2
H11b	124.74	131.2	123.0	129.5	124.2	130.0	138.2	130.8	118.7
H12	149.12	151.6	138.6	149.1	138.4	150.0	150.0	150.9	136.5
H13	124.2	129.5	120.6	128.1	126.8	128.3	143.2	129.3	117.9
H14	129.82	134.8	123.4	133.2	127.4	133.5	138.0	134.5	122.4
H15a	130.96	134.5	124.7	133.2	122.2	133.3	135.0	134.2	121.1
H15b	129.94	134.5	124.6	132.9	128.6	133.1	135.4	134.2	122.3
H16	146.36	152.5	138.5	150.6	138.7	151.2	151.8	152.1	137.5
H17a/b	134.12	135.4	124.8	133.9	126.1	134.0	137.0	135.1	122.3
H17b/a	134.12	139.3	128.3	137.8	124.8	138.0	136.7	139.0	125.5
H18a	145.92	150.1	136.2	148.2	132.5	148.7	143.6	149.6	133.3
H18b	130.24	134.0	123.3	132.6	122.9	132.4	140.2	133.8	118.2
H2	159.8	166.2	148.9	163.5	141.2	164.4	140.7	165.7	149.1
H20a	138.16	142.7	131.5	140.8	132.9	141.5	144.7	142.3	129.0
H20b	137.86	141.8	129.2	140.1	126.8	140.4	138.1	141.4	126.4
H22	158.4	164.7	149.0	161.7	141.1	162.9	149.9	164.2	147.4
H23a	136.64	139.4	127.5	137.6	129.1	137.7	139.4	138.9	124.5
H23b	144.42	149.4	135.6	147.2	134.1	148.2	146.3	148.8	132.3
H3	158.6	164.9	147.9	162.1	140.1	163.2	140.6	164.3	147.9
H4	168.26	177.9	160.8	175.5	150.6	176.4	152.5	177.6	159.6
H8	144.94	149.5	137.1	148.1	138.1	148.4	156.3	149.3	135.4
RMSD, Hz		5.23	8.11	3.41	11.26	3.91	10.08	4.84	10.27
ΔJ, Hz		-4.92	7.71	-2.99	9.42	-3.49	-0.78	-4.52	10.05

Protons	Exp.	b3lyp/6-311g(2d,2p)		b3lyp/6-311g(2df,3pd)		b3lyp/6-311g(3df,3pd)		b3lyp/aug-cc-pVTZ	
		mixed	spinspin	mixed	spinspin	mixed	spinspin	mixed	spinspin
H1	158.36	161.3	141.4	161.4	147.8	161.5	149.5	162.5	151.7
H11a	134.16	140.6	125.5	140.9	129.1	140.8	129.6	141.6	120.9
H11b	124.74	130.6	120.4	130.9	121.2	130.9	120.1	131.7	112.0
H12	149.12	150.7	133.7	151.0	137.7	150.9	136.9	152.1	129.1
H13	124.2	129.2	116.8	129.4	119.2	129.3	116.4	129.9	108.0
H14	129.82	134.3	118.8	134.6	122.4	134.5	122.2	135.3	115.2
H15a	130.96	134.1	121.7	134.3	122.8	134.2	121.5	134.9	113.0
H15b	129.94	134.0	121.0	134.3	123.1	134.2	121.8	135.0	114.3
H16	146.36	151.9	133.7	152.3	138.4	152.1	137.7	153.0	131.8
H17a/b	134.12	135.0	121.4	135.3	123.8	135.2	122.7	135.9	116.4
H17b/a	134.12	138.8	123.6	139.1	127.1	139.0	127.0	139.7	119.9
H18a	145.92	149.4	130.9	149.9	136.2	149.7	136.4	150.6	130.5
H18b	130.24	133.6	120.5	133.9	121.8	133.9	120.2	134.6	114.1
H2	159.8	165.1	144.9	165.4	151.8	165.4	154.7	166.6	152.7
H20a	138.16	142.0	127.7	142.3	129.9	142.3	129.3	143.1	121.9
H20b	137.86	141.2	125.9	141.6	128.9	141.5	128.7	142.3	117.5
H22	158.4	163.8	143.8	164.0	150.3	164.0	152.0	165.1	150.6
H23a	136.64	138.7	125.0	139.0	127.0	139.0	126.5	139.8	120.3
H23b	144.42	148.5	129.3	149.0	135.6	148.9	136.3	149.8	126.7
H3	158.6	163.7	143.9	164.0	150.8	164.0	153.3	165.3	150.6
H4	168.26	177.2	156.7	177.2	163.2	177.2	165.6	178.3	164.5
H8	144.94	149.1	131.7	149.3	135.4	149.2	134.8	149.9	129.7
RMSD, Hz		4.60	12.26	4.84	8.21	4.78	8.32	5.61	14.67
ΔJ, Hz		-4.27	11.89	-4.54	7.98	-4.47	7.98	-5.34	13.99

Protons	Exp.	b3lyp/aug-cc-pVTZ-J		pw91/aug-cc-pVTZ-J		pbe/aug-cc-pVTZ-J		b3lyp/6-31G-J
		mixed	spinspin	mixed	spinspin	mixed	spinspin	spinspin
H1	158.36	166.0	166.2	152.8	153.3	151.5	151.7	169.4
H11a	134.16	144.6	144.8	133.2	133.5	132.0	132.1	148.0
H11b	124.74	134.3	134.3	122.2	122.3	121.0	120.9	139.9
H12	149.12	155.1	155.2	142.3	142.5	141.1	141.0	158.2
H13	124.2	132.4	132.5	120.8	121.0	119.7	119.6	137.0
H14	129.82	137.8	138.1	126.7	126.9	125.6	125.6	141.7
H15a	130.96	137.5	137.7	126.2	126.5	125.2	125.1	141.8
H15b	129.94	137.7	137.7	126.2	126.3	125.1	125.0	141.4
H16	146.36	156.0	156.3	144.2	144.5	143.0	143.0	160.8
H17a/b	134.12	138.7	138.7	126.9	127.1	125.9	125.8	142.8
H17b/a	134.12	142.4	142.7	131.2	131.4	130.1	130.0	146.6
H18a	145.92	153.7	153.9	141.7	142.0	140.5	140.5	157.5
H18b	130.24	137.1	137.4	124.9	125.2	123.9	123.9	140.6
H2	159.8	170.3	170.4	157.0	157.5	155.6	155.8	173.4
H20a	138.16	146.0	146.1	133.9	134.0	132.7	132.6	150.4
H20b	137.86	145.0	145.4	133.3	133.5	132.1	132.2	148.6
H22	158.4	168.6	168.8	154.6	154.9	153.1	153.2	172.4
H23a	136.64	142.7	142.5	129.2	129.3	128.1	128.0	145.2
H23b	144.42	152.9	153.2	140.3	140.7	139.1	139.2	157.7
H3	158.6	169.0	169.0	155.9	156.3	154.5	154.7	172.0
H4	168.26	182.2	182.3	167.8	168.2	166.3	166.4	186.2
H8	144.94	152.7	152.9	140.3	140.4	139.1	139.0	158.6
RMSD, Hz		8.58	8.73	4.35	4.13	5.45	5.46	12.51
ΔJ, Hz		-8.34	-8.50	3.98	3.71	5.18	5.18	-12.32

Protons	Exp.	b3lyp/6-31G-J //b3lyp-31G-J	b3lyp/6-31+G*-J	b3lyp/6-311++G**-J	b3lyp/pcJ-0	
		spinspin	spinspin	spinspin	mixed	spinspin
H1	158.36	169.7	167.7	167.5	151.6	149.5
H11a	134.16	148.2	146.6	146.2	128.2	124.1
H11b	124.74	140.5	136.5	136.2	122.1	118.6
H12	149.12	161.1	156.9	156.7	136.0	131.6
H13	124.2	137.4	134.5	134.3	119.1	115.5
H14	129.82	141.9	139.8	139.6	124.3	119.9
H15a	130.96	141.9	139.7	139.4	123.3	119.6
H15b	129.94	141.5	139.5	139.2	123.2	119.0
H16	146.36	163.3	158.2	157.9	139.9	134.9
H17a/b	134.12	143.2	140.6	140.1	124.3	120.4
H17b/a	134.12	146.7	144.6	144.3	127.5	124.2
H18a	145.92	159.4	155.5	155.2	134.7	130.1
H18b	130.24	141.0	138.8	138.8	121.1	117.8
H2	159.8	173.2	171.7	171.6	154.0	151.5
H20a	138.16	152.4	148.2	147.8	130.7	126.1
H20b	137.86	148.7	146.9	146.7	128.8	124.7
H22	158.4	171.8	170.4	170.2	152.0	149.0
H23a	136.64	147.5	144.3	144.0	124.3	120.5
H23b	144.42	160.3	155.2	154.7	133.6	128.6
H3	158.6	172.5	170.4	170.3	152.5	150.0
H4	168.26	186.4	184.1	183.7	167.9	166.0
H8	144.94	161.3	155.2	154.8	139.5	136.1
RMSD, Hz		13.41	10.47	10.19	7.87	11.51
ΔJ, Hz		-13.22	-10.27	-10.00	7.30	10.98

Protons	Exp.	B3LYP/pcJ-0 //B3LYP/pcJ-0	B3LYP/pcJ-1		B3LYP/pcJ-1 //B3LYP/pcJ-1	B3LYP/pcJ-2	B3LYP/pcJ-2_2006
		spinspin	mixed	spinspin	spinspin	spinspin	spinspin
H1	158.36	149.4	166.2	163.9	163.1	164.4	166.7
H11a	134.16	123.2	144.6	144.1	143.1	143.2	145.3
H11b	124.74	118.1	134.3	134.4	133.6	133.2	135.1
H12	149.12	133.1	153.8	153.0	152.2	153.7	156.0
H13	124.2	117.8	132.0	132.0	131.5	131.4	133.3
H14	129.82	119.1	137.8	137.1	136.5	136.8	138.8
H15a	130.96	119.8	137.9	137.5	137.0	136.5	138.4
H15b	129.94	118.7	137.5	137.3	136.6	136.5	138.5
H16	146.36	137.9	155.7	154.3	154.2	154.7	157.0
H17a/b	134.12	121.0	138.4	138.1	137.7	137.4	139.4
H17b/a	134.12	125.1	142.7	142.2	141.8	141.3	143.3
H18a	145.92	132.9	153.7	152.2	151.8	152.3	154.5
H18b	130.24	118.9	136.5	136.2	135.9	136.0	138.0
H2	159.8	151.5	170.4	168.2	167.4	168.5	170.9
H20a	138.16	128.5	145.9	145.2	144.8	144.8	146.9
H20b	137.86	125.5	144.9	144.2	143.6	143.8	145.9
H22	158.4	148.1	168.3	166.1	165.0	167.0	169.3
H23a	136.64	121.8	141.9	141.4	140.9	141.3	143.4
H23b	144.42	131.3	153.0	151.5	151.4	151.5	153.7
H3	158.6	150.9	169.1	166.9	166.2	167.2	169.5
H4	168.26	167.2	182.4	180.4	179.5	180.3	182.8
H8	144.94	141.4	152.7	151.8	151.7	151.6	153.7
RMSD, Hz		10.48	8.49	7.46	6.89	7.24	9.34
ΔJ, Hz		9.00	-8.21	-7.22	-6.65	-7.01	-9.14

Protons	Exp.	b3lyp/tzvp		b3lyp/tzvp//b3lyp/tzvp	b3lyp/epr-III//b3lyp/aug-cc-pVDZ	
		mixed	spinspin	spinspin	mixed	spinspin
H1	158.36	163.2	155.3	154.2	165.2	162.1
H11a	134.16	142.0	134.4	134.4	144.3	141.4
H11b	124.74	132.2	123.6	122.1	132.8	130.1
H12	149.12	152.1	143.8	143.3	153.8	150.8
H13	124.2	130.3	122.4	121.3	130.6	128.0
H14	129.82	135.6	128.1	127.1	136.4	133.8
H15a	130.96	135.4	126.4	125.6	136.5	133.7
H15b	129.94	135.2	126.9	126.2	136.7	134.0
H16	146.36	153.5	145.8	145.4	154.8	151.8
H17a/b	134.12	136.2	127.9	127.5	138.0	135.3
H17b/a	134.12	140.2	131.8	131.2	141.6	138.8
H18a	145.92	150.8	143.2	142.8	152.8	149.8
H18b	130.24	134.7	126.2	125.7	136.5	133.7
H2	159.8	167.2	160.2	159.0	169.3	166.1
H20a	138.16	143.5	135.0	134.3	145.5	142.5
H20b	137.86	142.5	134.0	133.3	144.2	141.3
H22	158.4	165.5	157.8	156.8	167.6	164.4
H23a	136.64	139.8	130.8	130.2	142.2	139.4
H23b	144.42	150.2	142.4	142.1	152.3	149.3
H3	158.6	165.9	158.9	158.0	168.1	165.0
H4	168.26	179.1	171.6	170.0	181.1	177.8
H8	144.94	150.5	142.6	141.9	151.3	148.3
RMSD, Hz		6.05	3.19	3.69	7.62	4.82
ΔJ, Hz		-5.75	2.27	3.03	-7.37	-4.46

Protons	Exp.	B3LYP/epr-III		pbe/NMR-DKH		pbe/ccJ-pVDZ	B3PW91/6-311++G(d,p)// B3PW91/6-311++G(d,p)	
		mixed	spinspin	mixed	spinspin	spinspin	mixed	spinspin
H1	158.36	164.4	161.3	150.3	143.3	149.2	151.2	136.6
H11a	134.16	143.3	140.5	130.6	125.2	130.7	131.4	121.1
H11b	124.74	133.2	130.6	119.9	115.2	120.1	119.7	111.9
H12	149.12	153.8	150.8	139.8	133.7	138.7	140.2	129.3
H13	124.2	131.5	128.9	118.8	114.0	118.9	119.4	111.0
H14	129.82	136.8	134.2	124.5	119.3	124.3	124.6	115.1
H15a	130.96	136.5	133.8	124.0	118.6	124.5	124.6	115.6
H15b	129.94	136.6	133.9	124.0	118.7	124.2	124.5	115.3
H16	146.36	154.7	151.7	141.8	135.9	140.8	141.8	129.9
H17a/b	134.12	137.5	134.8	124.8	119.4	124.9	125.6	115.9
H17b/a	134.12	141.4	138.6	128.8	123.3	129.1	129.5	119.8
H18a	145.92	152.3	149.3	139.2	133.1	138.6	139.5	127.8
H18b	130.24	136.2	133.4	122.7	117.2	122.6	123.7	113.7
H2	159.8	168.5	165.4	154.4	147.2	153.2	154.9	139.8
H20a	138.16	144.8	141.9	131.7	125.9	131.4	132.2	121.8
H20b	137.86	143.9	141.1	130.7	124.8	130.7	131.2	120.2
H22	158.4	167.0	163.8	151.9	144.7	150.6	153.6	139.1
H23a	136.64	141.4	138.6	127.3	121.5	126.9	128.3	118.2
H23b	144.42	151.6	148.6	137.8	131.7	137.1	138.7	127.0
H3	158.6	167.1	164.0	153.3	146.1	152.1	153.8	138.8
H4	168.26	180.3	176.9	164.8	157.5	164.3	165.8	150.2
H8	144.94	151.6	148.6	137.9	132.1	137.4	138.4	128.6
RMSD, Hz		7.29	4.49	6.59	12.43	7.00	5.95	17.09
ΔJ, Hz		-7.07	-4.16	6.38	12.30	6.77	5.73	16.92

[a] *J*-couplings were calculated in two approximations, *mixed* and *spinspin* (see text for details). Unless otherwise stated the geometry of strychnine was optimized at the B3LYP/6-31G(d) level;
$\Delta J = \overline{J^{exp}} - \overline{J^{calc}}$

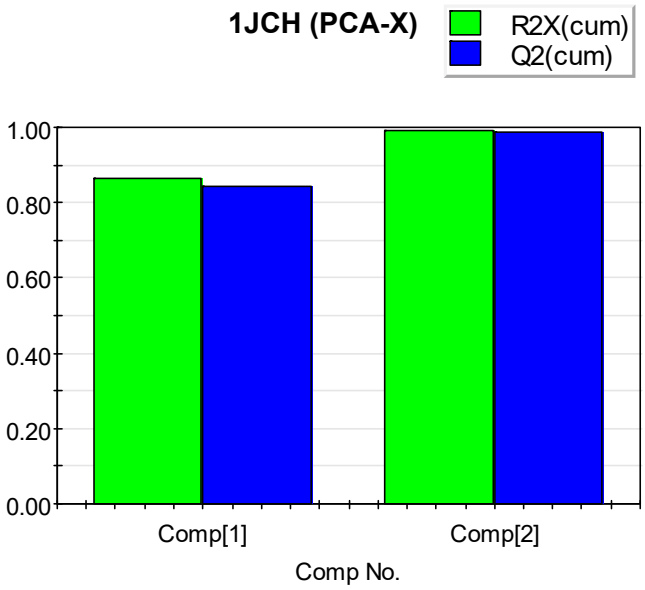
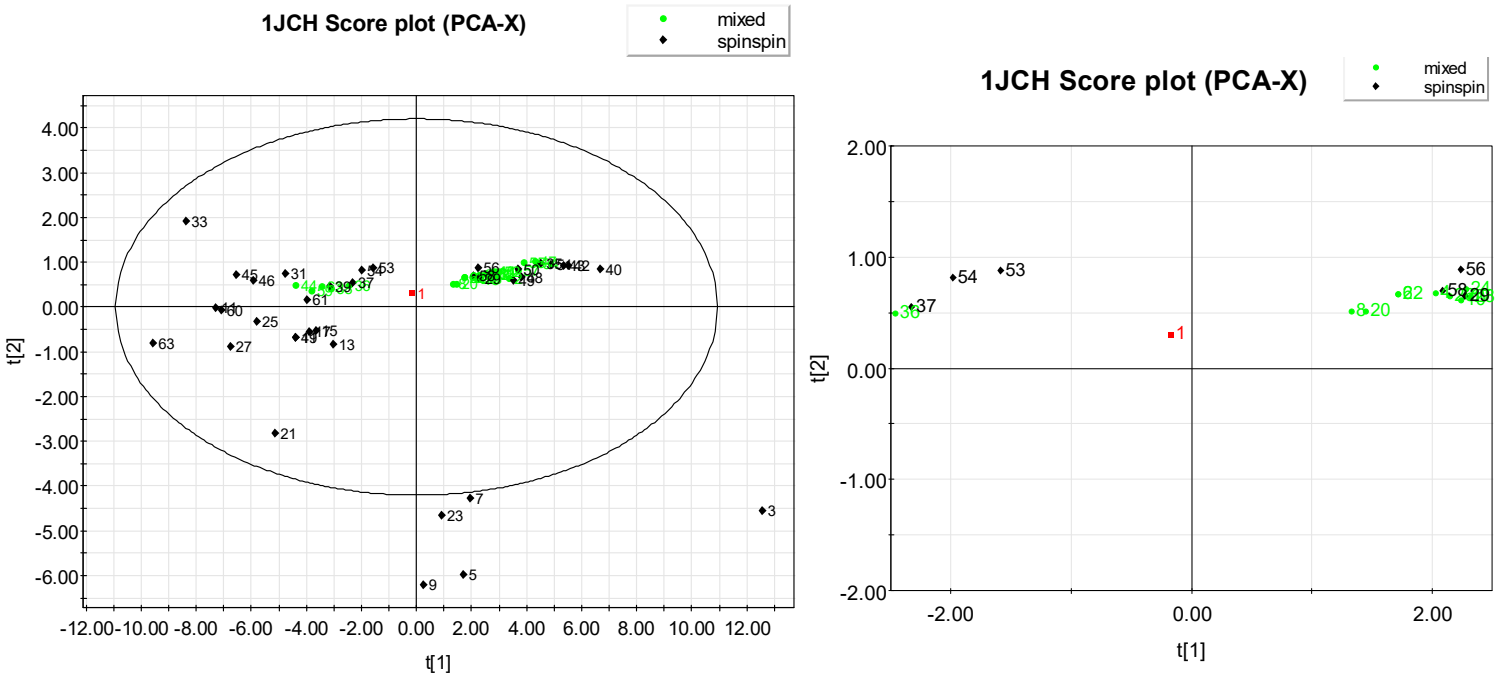


Figure 2S. Summary of Principal Component Analysis (PCA) of 62 combination of functional/basis sets used to calculate 22 $^{1}J_{CH}$ couplings of strychnine and the set of experimental *J*-couplings. Unless otherwise stated the 3D structure of strychnine was optimized at the B3LYP/6-31G(d) level. R2X(cum) is a fraction of the variation of the data explained after each component and Q2X(cum) is a cross-validated R2X(cum). The two-components RCA accounts for 99.1% of data variations (R2X(cum)).



	Model		Model		Model
1	Experimental data	22	b3lyp/6-31+g(d,p)-m	43	b3lyp/6-311++g(d,p)-J-ss
2	b3lyp/6-31g-m	23	b3lyp/6-31+g(d,p)-ss	44	b3lyp/pcJ-0-m
3	b3lyp/6-31g-ss	24	b3lyp/6-311g(3d,2p)-m	45	b3lyp/pcJ-0-ss
4	b3lyp/6-31g(d)-m	25	b3lyp/6-311g(3d,2p)-ss	46	b3lyp/pcJ-0//B3LYP/pcJ-0-ss
5	b3lyp/6-31g(d)-ss	26	b3lyp/6-311g(2d,2p)-m	47	b3lyp/pcJ-1-m
6	b3lyp/6-31+g(d)-m	27	b3lyp/6-311g(2d,2p)-ss	48	b3lyp/pcJ-1-ss
7	b3lyp/6-31+g(d)-ss	28	b3lyp/6-311g(d,3pd)-m	49	b3lyp/pcJ-1//B3LYP/pcJ-1-ss
8	b3lyp/6-31g(d,p)-m	29	b3lyp/6-311g(d,3pd)-ss	50	b3lyp/pcJ-2-ss
9	b3lyp/6-31g(d,p)-ss	30	b3lyp/6-31g(3df,3pd)-m	51	b3lyp/pcJ-2_2006-ss
10	b3lyp/6-311g(2df,2pd)-m	31	b3lyp/6-31g(3df,3pd)-ss	52	b3lyp/tzvp-m
11	b3lyp/6-311g(2df,2pd)-ss	32	b3lyp/aug-cc-pVTZ-m	53	b3lyp/tzvp-ss
12	b3lyp/6-311g(d,p)-m	33	b3lyp/aug-cc-pVTZ-ss	54	b3lyp/tzvp//b3lyp/tzvp-ss
13	b3lyp/6-311g(d,p)-ss	34	b3lyp/aug-cc-pVTZ-J-m	55	b3lyp/epr-III//b3lyp/aug-cc-pVDZ-m
14	b3lyp/6-311+g(d,p)-m	35	b3lyp/aug-cc-pVTZ-J-ss	56	b3lyp/epr-III//b3lyp/aug-cc-pVDZ-ss
15	b3lyp/6-311+g(d,p)-ss	36	pw91/aug-cc-pVTZ-J-m	57	b3lyp/epr-III-m
16	b3lyp/6-311++g(d,p)-m	37	pw91/aug-cc-pVTZ-J-ss	58	b3lyp/epr-III-ss
17	b3lyp/6-311++g(d,p)-ss	38	pbe/aug-cc-pVTZ-J-m	59	pbe/NMR-DKH-m
18	b3lyp/6-311+g(2d,p)-m	39	pbe/aug-cc-pVTZ-J-ss	60	pbe/NMR-DKH-ss
19	b3lyp/6-311+g(2d,p)-ss	40	b3lyp/6-31g-J-ss	61	pbe/ccJ-pVDZ-ss
20	b3lyp/6-31g(d,3pd)-m	41	b3lyp/6-31g-J//b3lyp/6-31g-J-ss	62	B3PW91/6-311++g(d,p)// B3PW91/6-311++g(d,p)-m
21	b3lyp/6-31g(d,3pd)-ss	42	b3lyp/6-31+g(d)-J-ss	63	B3PW91/6-311++g(d,p)// B3PW91/6-311++g(d,p)-ss

Figure 3S. Score plot of two new vectors, t1 vs t2, describing 99.1% variations among 62 different combination of functional/basis sets used to calculate 22 $^{1}J_{CH}$ couplings of strychnine and the set of experimental $^{1}J_{CH}$ couplings. Unless otherwise stated the 3D structure of strychnine was optimized at the B3LYP/6-31G(d) level. M and ss suffixes denote mixed and spinspin methods of *J*-coupling calculation. Experimental *J*-couplings (**1**) are best approximated by model chemistries 8, 20 and 53 which is consistent with RMSD data (see Table 1S).

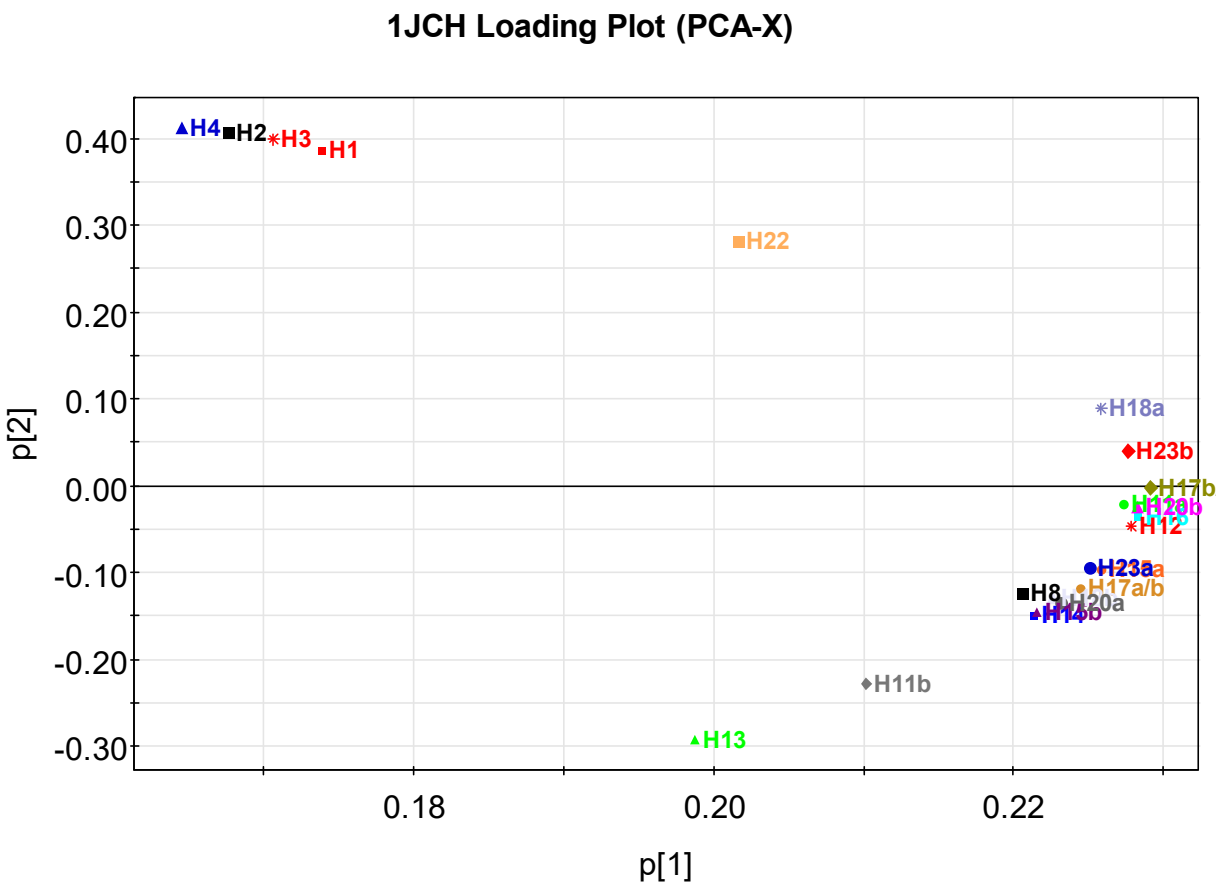


Figure 4S. Loading plot of p1 vs p2 showing which *J*-couplings describe the similarities and dissimilarities between different combinations of functional/basis sets used to calculate 22 $^{1}J_{CH}$ couplings of strychnine and the set of experimental $^{1}J_{CH}$ couplings. Largest differences are seen for *J*-couplings of aromatic protons (H1-H4), aliphatic H22 and protons H13, H11b.

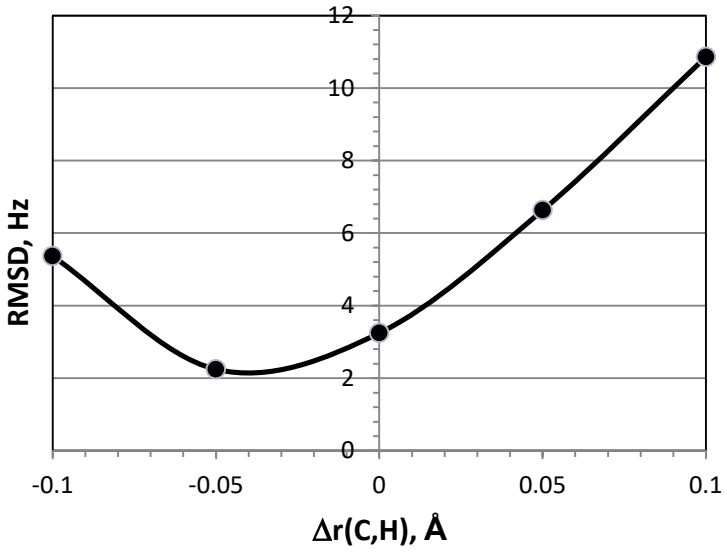


Figure 5S. RMSD of $^{1}J_{CH}$ couplings of strychnine (B3LYP/6-31G(d,p)(mixed)) as a function of the C-H distance deviations (Δr(C,H)) from the C-H distances calculated at the B3LYP/6-31G(d) level of theory.

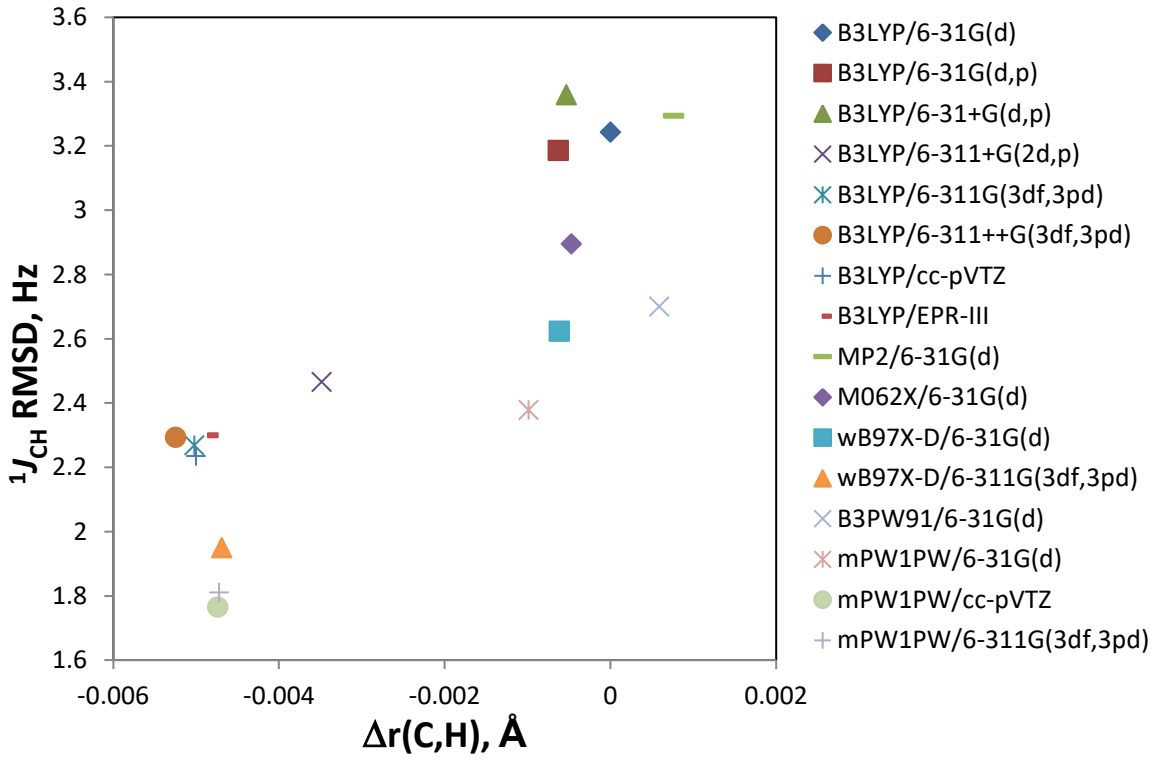


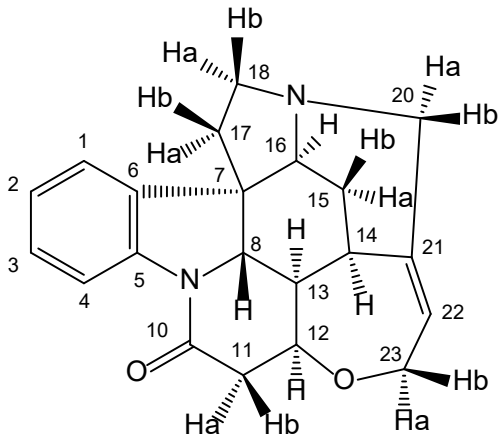
Figure 6S. RMSD of $^1J_{CH}$ couplings of strychnine (B3LYP/6-31G(d,p)(mixed)) as a function of the average C-H distance deviations (Δr(C,H)) from the C-H distances calculated at the B3LYP/6-31G(d) level of theory for 16 different geometry optimization models.

Table 3S. RMSD and differences between mean values of experimental and calculated *J*-couplings (ΔJ) for 22 $^1J_{CH}$ couplings of strychnine calculated at B3LYP/6-31G(d,p)(mixed) and B3LYP/TZVP(spinspin) levels[a] for strychnine geometries optimized by 16 different methods.

Geometry optimization methods	B3LYP/6-31G(d,p)		B3LYP/TZVP	
	RMSD, Hz	ΔJ, Hz[b]	RMSD, Hz	ΔJ, Hz[b]
B3LYP/6-31G(d)	3.24	-2.77	3.17	2.27
B3LYP/6-31G(d,p)	3.19	-2.70	3.23	2.33
B3LYP/6-31+G(d,p)	3.36	-2.89	3.15	2.14
B3LYP/6-311+G(2d,p)	2.47	-1.88	3.70	3.06
B3LYP/6-311G(3df,3pd)	2.27	-1.57	3.92	3.32
B3LYP/6-311++G(3df,3pd)	2.29	-1.60	3.91	3.28
B3LYP/cc-pVTZ	2.24	-1.56	3.92	3.33
B3LYP/EPR-III	2.30	-1.63	3.90	3.27
MP2/6-31G(d)	3.29	-2.71	3.37	2.37
M062x/6-31G(d)	2.89	-2.25	3.61	2.79
ωB97XD/6-31G(d)	2.62	-1.96	3.81	3.07
ωB97XD/6-311G(3df,3pd)	1.95	-0.85	4.60	4.06
B3PW91/6-31G(d)	2.70	-2.06	3.78	3.00
mPW1PW/6-31G(d)	2.38	-1.59	4.12	3.41
mPW1PW/6-311G(3df,3pd)	1.81	-0.51	4.90	4.39
mPW1PW/cc-pVTZ	1.77	-0.51	4.90	4.39

[a] mixed and spinspin type of calculations were used for B3LYP/6-31G(d,p) and B3LYP/TZVP levels of theory, respectively; [b] $\Delta J = \overline{J^{exp}} - \overline{J^{calc}}$

Table 4S. $^{1}J_{CH}$ Couplings, RMSD and differences between mean values of experimental and calculated *J*-couplings (ΔJ) for 22 $^{1}J_{CH}$ couplings of strychnine calculated at the B3LYP/6-31G(d,p) level[a] for strychnine geometries optimized by 15 different methods.



Proton	Exp.	B3LYP/6-31G(d,p)	B3LYP/6-31+G(d,p)	B3LYP/6-311+G(2d,p)	B3LYP/6-311G(3df,3pd)	B3LYP/6-311++G(3df,3pd)	B3LYP/cc-pVTZ	B3LYP/EPR-III	MP2/6-31G(d)
H1	158.36	160.0	160.3	158.8	158.3	158.4	158.4	158.6	161.2
H11a	134.16	140.1	140.7	139.9	139.5	139.9	139.5	139.9	139.1
H11b	124.74	129.9	129.7	128.8	128.7	128.3	128.5	128.3	130.7
H12	149.12	149.1	149.1	148.1	147.6	147.7	147.8	147.8	149.9
H13	124.2	128.1	127.9	127.2	127.3	127.2	127.1	127.0	127.9
H14	129.82	133.3	133.2	132.4	132.2	132.1	132.1	132.1	132.9
H15a	130.96	133.7	133.6	132.9	132.8	132.8	132.7	132.7	132.9
H15b	129.94	133.3	133.4	132.6	132.3	132.3	132.3	132.3	132.7
H16	146.36	150.7	150.9	149.9	149.7	149.8	149.7	149.8	149.1
H17a/b	134.12	134.2	134.6	133.8	133.6	133.7	133.5	133.6	134.5
H17b/a	134.12	138.4	138.4	137.7	137.5	137.5	137.5	137.5	138.1
H18a	145.92	148.6	149.0	147.9	147.7	147.7	147.7	147.8	147.4
H18b	130.24	132.9	133.0	132.5	132.1	132.1	132.1	132.1	133.8
H2	159.8	163.7	164.1	162.5	162.1	162.2	162.1	162.2	163.4
H20a	138.16	141.4	141.8	140.6	140.6	140.5	140.5	140.6	141.4
H20b	137.86	140.6	140.6	139.9	139.6	139.6	139.6	139.6	139.8
H22	158.4	162.0	162.3	160.9	160.3	160.5	160.4	160.6	163.7
H23a	136.64	137.9	138.2	137.5	136.8	136.9	137.0	137.0	139.2
H23b	144.42	147.8	148.3	147.2	147.1	147.1	147.1	147.2	146.3
H3	158.6	162.3	162.8	161.4	160.7	160.9	160.9	161.1	162.3
H4	168.26	176.2	176.6	174.5	174.1	174.1	174.1	174.2	177.8
H8	144.94	148.3	148.3	147.4	147.2	147.1	147.1	147.0	148.7
RMSD, Hz		3.19	3.36	2.47	2.27	2.29	2.24	2.30	3.29
ΔJ, Hz[b]		-2.70	-2.89	-1.88	-1.57	-1.60	-1.56	-1.63	-2.71

Proton	Exp.	M062x/6-31G(d)	ωB97X-D/6-31G(d)	ωB97X-D/6-311G(3df,3pd)	B3PW91/6-31G(d)	mPW1PW/6-31G(d)	mPW1PW/6-311G (3df,3pd)	mPW1PW/cc-pVTZ	mPW1PW/cc-pVTZ[c]
H1	158.36	159.6	159.4	157.8	159.6	159.1	157.6	157.7	158.9
H11a	134.16	140.3	139.9	139.8	139.4	139.0	138.7	138.7	137.6
H11b	124.74	129.1	129.1	127.6	129.1	128.6	127.2	127.0	126.2
H12	149.12	148.2	148.0	146.6	148.1	147.5	146.0	146.2	147.9
H13	124.2	127.8	127.5	126.5	127.6	127.2	126.2	126.1	126.0
H14	129.82	132.9	132.6	131.4	132.4	132.0	130.8	130.7	131.5
H15a	130.96	133.4	133.2	132.3	133.2	132.8	131.9	131.9	131.3
H15b	129.94	133.0	132.9	132.0	132.8	132.4	131.5	131.5	131.7
H16	146.36	149.4	149.1	148.1	149.5	148.9	147.9	147.9	147.6
H17a/b	134.12	134.2	134.0	133.3	133.9	133.6	132.9	132.9	132.0
H17b/a	134.12	138.6	138.2	137.3	138.0	137.7	136.9	136.9	136.4
H18a	145.92	148.1	148.0	147.1	147.8	147.3	146.6	146.6	146.1
H18b	130.24	132.5	132.1	131.2	132.4	132.0	131.2	131.2	131.1
H2	159.8	162.8	162.7	161.2	163.3	162.7	161.3	161.3	161.8
H20a	138.16	140.9	140.5	139.5	140.7	140.2	139.3	139.3	138.8
H20b	137.86	140.2	139.8	138.9	139.8	139.3	138.5	138.4	138.1
H22	158.4	162.4	161.9	160.4	162.0	161.6	160.1	160.2	160.3
H23a	136.64	136.9	136.8	135.6	137.2	136.6	135.4	135.7	135.9
H23b	144.42	146.8	146.6	145.9	146.7	146.0	145.4	145.4	145.1
H3	158.6	161.2	161.3	159.7	161.9	161.2	159.7	159.9	159.8
H4	168.26	176.1	175.5	173.6	176.0	175.5	173.7	173.6	171.3
H8	144.94	148.3	147.3	146.1	147.2	146.7	145.6	145.5	145.4
RMSD, Hz		2.89	2.62	1.95	2.70	2.38	1.81	1.77	1.60
ΔJ, Hz[b]		-2.25	-1.96	-0.85	-2.06	-1.59	-0.51	-0.51	-0.99

[a] *J*-Couplings were calculated with mixed method; [b] $\Delta J = \overline{J^{exp}} - \overline{J^{calc}}$; [c] *J*-couplings were calculated at the B3LYP/6-31G(d,p) level of theory using the polarizable continuum model (PCM) for chloroform.

Table 5S. Experimental and DFT calculated 119 $^{1}J_{CH}$ couplings for 62 compounds[a]

Compound	Experimental,[a] Hz	Calculated,[b] Hz	ΔJ,[c] Hz
1,1-dibromoethene	167.0	170.3	3.3
1,2,3-triazole	194.0	195.2	1.2
1,2-difluorobenzene	163.9	163.3	-0.6
	163.8	163.3	-0.4
1,3,4-triazole	209.0	212.4	3.4
1,3,5-triazine	207.2	206.7	-0.5
1,3-difluorobenzene	163.6	162.5	-1.2
	165.3	166.3	1.0
	165.5	166.8	1.3
5,5-dimethyl-13-dioxane	167.5	168.3	0.8
	157.4	153.5	-3.9
5-methylenenorbornene	130.7	131.0	0.3
	131.4	132.4	1.0
	136.0	137.9	1.9
	136.8	138.7	1.9
	147.7	147.6	-0.1
	148.3	149.3	1.0
	155.1	158.9	3.8
	157.0	160.2	3.2
	168.9	171.4	2.5
	170.8	173.8	3.0
acetaldehyde	172.4	168.3	-4.1
acetonitrile	136.2	135.8	-0.4
acetophenone	127.3	128.7	1.4
acetylene	248.7	261.4	12.7
acrylonitrile	165.4	166.1	0.7
	163.1	166.7	3.6
	176.7	173.0	-3.7
allene	167.8	171.6	3.8
alpha-pinene	127.0	127.4	0.4
	127.0	127.7	0.7
	137.0	137.0	0.0
	137.0	142.9	5.9
	144.0	143.0	-1.0
	144.0	144.2	0.2
	158.0	159.9	1.9
anthracene	159.5	158.8	-0.7
benzaldehyde	173.7	170.9	-2.8
benzene	159.0	159.1	0.1
bromoethene	160.0	163.1	3.1
	163,7	167.7	4.0
carene	125.0	124.6	-0.4
	125.0	125.6	0.6
	125.0	126.3	1.3
	125.0	127.4	2.4

Compound	Experimental,[a] Hz	Calculated,[b] Hz	ΔJ,[c] Hz
carene	160.9	164.3	3.4
	162.6	166.3	3.6
	159.0	156.8	-2.2
chloroethene	153.8	156.2	2.4
	167.1	175.5	8.4
cis-1-chloropropene	180.0	181.5	1.5
cubane	134.0	132.2	-1.8
cyanoallene	137.2	138.4	1.3
	168.6	171.4	2.8
cyclobutane	122.4	124.1	1.7
cyclobutene	126.4	128.5	2.1
	162.0	162.5	0.5
	160.0	162.5	2.5
cyclohexane	167.0	170.0	3.0
cyclopropane	184.5	179.0	-5.5
	125.3	126.6	1.3
cyclopropene	156.3	159.3	3.0
difluoromethane	159.5	157.7	-1.8
ethane	159.5	158.6	-0.9
ethene	157.0	158.9	1.9
fluorene	159.0	159.3	0.3
	275.0	293.2	18.2
	162.2	163.1	0.9
	159.2	164.6	5.4
fluoroacetylene	200.2	196.4	-3.8
fluoroethene	149.1	147.1	-2.0
	172.0	176.2	4.2
	175.0	176.6	1.6
fluoromethane	202.0	203.7	1.7
formaldehyde	269.0	270.4	1.4
furan	189.0	189.6	0.6
	206.0	209.8	3.8
HCN	125.0	128.2	3.2
imidazole	140.0	137.3	-2.7
	132.6	130.6	-2.0
methane	133.9	131.1	-2.8
methylether	145.9	146.8	0.9
norbornene	166.9	170.0	3.1
	131.9	130.6	-1.3
	175.5	175.8	0.3
	154.8	156.4	1.6
norbornenone	160.5	159.1	-1.4
oxirane	248.0	263.3	15.3
o-xylene	159.5	162.4	2.9
	163.0	172.2	9.2
phenylacetylene	160.9	164.3	3.4
phenylallene	162.6	166.3	3.6
	159.0	156.8	-2.2

Compound	Experimental,[a] Hz	Calculated,[b] Hz	ΔJ,[c] Hz
prismane	180.0	185.7	5.7
propene	152.0	152.3	0.3
	153.3	157.0	3.7
	157.0	160.4	3.4
propyne	248.0	260.9	12.9
pyrazine	182.7	181.9	-0.8
pyrazole	177.0	178.5	1.5
	186.0	188.3	2.3
pyridazine	169.9	166.1	-3.8
	182.5	182.7	0.2
pyridine	162.4	161.3	-1.1
	163.0	162.5	-0.5
	177.6	178.8	1.1
pyrimidine	168.0	166.6	-1.4
	181.8	180.9	-0.9
	206.0	204.6	-1.4
pyrrole	169.0	172.7	3.7
	183.0	185.3	2.3
salicylaldehyde	159.4	158.4	-1.0
	160.3	159.0	-1.3
	162.6	164.7	2.1
	164.9	165.2	0.3
thiirane	170.5	172.8	2.3
tms	120.0	122.7	2.7
trichloroacetaldehyde	207.0	208.6	1.6
trifluoromethane	239.1	232.8	-6.3

[a] Experimental *J*-couplings from ref. 7. Assignments of individual couplings for each compound see in ref. 7;

[b] *J*-couplings were calculated at the B3LYP/6-31G(d,p)(mixed)//mPW1PW/cc-pVTZ level of theory; RMSD for all couplings except for four alkynes is 2.7 Hz (1.6%);

[c] $\Delta J = J^{calc} - J^{exp}$.

Table 6S. DFT-calculated $^{1}J_{CH}$ coupling (Hz) in acetylene using 18 x 18 combinations of geometry optimization and *J*-coupling model chemistries

J-coupling calculation	Geometry optimization																	
	b3lyp/ STO-3g	b3lyp/ 6-31g(d)	b3lyp/ 6-31g(d,p)	b3lyp/ 6-31+g(d)	b3lyp/ 6-31+g(d,p)	b3lyp/ 6-31++g(d)	b3lyp/6-31++g(d,p)	b3lyp/6-311g(d)	b3lyp/6-311g(d,p)	b3lyp/6-311+g(d)	b3lyp/6-311+g(d,p)	b3lyp/6-311++g(d)	b3lyp/6-311++g(d,p)	b3lyp/cc-pVDZ	b3lyp/cc-pVTZ	b3lyp/aug-cc-pVDZ	b3lyp/aug-cc-pVTZ	b3lyp/aug-cc-pVTZ-J
b3lyp/STO-3g	200.0	197.8	197.7	198.3	198.2	198.3	198.2	196.6	196.1	196.8	196.4	196.8	196.4	199.6	195.6	199.3	195.7	195.7
b3lyp/6-31g(d)	210.6	207.1	206.9	208.2	208.0	208.2	208.0	204.6	203.8	205.1	204.3	205.1	204.3	210.5	202.8	209.9	202.8	202.9
b3lyp/6-31g(d,p)	201.7	196.7	196.4	197.9	197.6	197.9	197.6	193.7	192.7	194.2	193.2	194.2	193.2	200.8	191.4	200.0	191.5	191.6
b3lyp/6-31+g(d)	218.1	214.8	214.6	215.9	215.7	215.9	215.7	212.2	211.5	212.7	212.0	212.7	212.0	218.1	210.4	217.6	210.5	210.6
b3lyp/6-31+g(d,p)	209.1	204.3	204.0	205.6	205.2	205.6	205.2	201.3	200.3	201.8	200.8	201.8	200.8	208.4	199.0	207.7	199.1	199.2
b3lyp/6-31++g(d)	220.9	217.7	217.5	218.8	218.6	218.8	218.6	215.1	214.4	215.6	214.9	215.6	214.9	221.0	213.3	220.4	213.4	213.5
b3lyp/6-31++g(d,p)	211.9	207.2	206.9	208.4	208.1	208.4	208.1	204.2	203.2	204.7	203.7	204.7	203.7	211.3	201.9	210.5	202.0	202.1
b3lyp/6-311g(d)	256.6	255.3	255.3	256.1	256.1	256.1	256.1	253.4	252.9	253.7	253.3	253.7	253.3	257.5	252.2	257.2	252.2	252.3
b3lyp/6-311g(d,p)	252.7	252.3	252.3	253.0	253.0	253.0	253.0	250.4	250.1	250.8	250.5	250.8	250.5	254.1	249.4	253.9	249.5	249.5
b3lyp/6-311+g(d)	257.2	256.0	255.9	256.8	256.8	256.8	256.8	254.0	253.6	254.4	254.0	254.4	254.0	258.2	252.8	257.9	252.9	252.9
b3lyp/6-311+g(d,p)	252.9	252.4	252.4	253.2	253.2	253.2	253.2	250.5	250.2	250.9	250.6	250.9	250.6	254.3	249.5	254.1	249.6	249.6
b3lyp/6-311++g(d)	256.9	255.7	255.6	256.5	256.4	256.5	256.5	253.7	253.3	254.1	253.7	254.1	253.7	257.9	252.5	257.6	252.6	252.6
b3lyp/6-311++g(d,p)	252.5	251.9	251.9	252.7	252.7	252.7	252.7	250.1	249.7	250.4	250.1	250.4	250.1	253.8	249.0	253.6	249.1	249.1
b3lyp/cc-pVDZ	225.2	222.6	222.5	223.5	223.4	223.6	223.4	220.4	219.7	220.8	220.2	220.8	220.1	225.4	218.8	225.0	218.9	219.0
b3lyp/cc-pVTZ	259.0	255.6	255.4	256.5	256.3	256.6	256.3	253.3	252.5	253.7	252.9	253.7	252.9	258.7	251.5	258.1	251.6	251.7
b3lyp/aug-cc-pVDZ	305.4	305.8	305.9	306.7	306.7	306.7	306.7	303.9	303.6	304.3	304.0	304.3	304.0	307.6	302.8	307.5	302.9	302.9
b3lyp/aug-cc-pVTZ	263.2	261.9	261.8	262.8	262.7	262.8	262.7	259.8	259.3	260.2	259.7	260.2	259.7	264.3	258.4	264.0	258.5	258.6
b3lyp/aug-cc-pVTZ-J	279.2	276.7	276.6	277.8	277.6	277.8	277.6	274.3	273.6	274.7	274.1	274.7	274.1	279.7	272.6	279.3	272.7	272.8

Table 7S. Differences between experimental (249 Hz) and DFT-calculated $^{1}J_{CH}$ coupling in acetylene using 18 x 18 combinations of geometry optimization and *J*-coupling model chemistries

J-coupling calculation	Geometry optimization																	
	b3lyp/ STO-3g	b3lyp/ 6-31g(d)	b3lyp/ 6-31g(d,p)	b3lyp/ 6-31+g(d)	b3lyp/ 6-31+g(d,p)	b3lyp/ 6-31++g(d)	b3lyp/6-31++g(d,p)	b3lyp/6-311g(d)	b3lyp/6-311g(d,p)	b3lyp/6-311+g(d)	b3lyp/6-311+g(d,p)	b3lyp/6-311++g(d)	b3lyp/6-311++g(d,p)	b3lyp/cc-pVDZ	b3lyp/cc-pVTZ	b3lyp/aug-cc-pVDZ	b3lyp/aug-cc-pVTZ	b3lyp/aug-cc-pVTZ-J
b3lyp/STO-3g	49.0	51.2	51.3	50.7	50.8	50.7	50.8	52.4	52.9	52.2	52.6	52.2	52.6	49.4	53.4	49.7	53.3	53.3
b3lyp/6-31g(d)	38.4	41.9	42.1	40.8	41.0	40.8	41.0	44.4	45.2	43.9	44.7	43.9	44.7	38.5	46.2	39.1	46.2	46.1
b3lyp/6-31g(d,p)	47.3	52.3	52.6	51.1	51.5	51.1	51.4	55.3	56.3	54.8	55.8	54.8	55.8	48.2	57.6	49.0	57.5	57.4
b3lyp/6-31+g(d)	30.9	34.2	34.4	33.1	33.3	33.1	33.3	36.8	37.5	36.3	37.0	36.3	37.0	30.9	38.6	31.4	38.5	38.4
b3lyp/6-31+g(d,p)	39.9	44.7	45.0	43.4	43.8	43.4	43.8	47.7	48.7	47.2	48.2	47.2	48.2	40.6	50.0	41.3	49.9	49.8
b3lyp/6-31++g(d)	28.1	31.3	31.5	30.2	30.4	30.2	30.4	33.9	34.6	33.4	34.1	33.4	34.1	28.0	35.7	28.6	35.6	35.5
b3lyp/6-31++g(d,p)	37.1	41.8	42.1	40.6	40.9	40.6	40.9	44.8	45.8	44.3	45.3	44.3	45.3	37.7	47.1	38.5	47.0	46.9
b3lyp/6-311g(d)	-7.6	-6.3	-6.3	-7.1	-7.1	-7.1	-7.1	-4.4	-3.9	-4.7	-4.3	-4.7	-4.3	-8.5	-3.2	-8.2	-3.2	-3.3
b3lyp/6-311g(d,p)	-3.7	-3.3	-3.3	-4.0	-4.0	-4.0	-4.0	-1.4	-1.1	-1.8	-1.5	-1.8	-1.5	-5.1	-0.4	-4.9	-0.5	-0.5
b3lyp/6-311+g(d)	-8.2	-7.0	-6.9	-7.8	-7.8	-7.8	-7.8	-5.0	-4.6	-5.4	-5.0	-5.4	-5.0	-9.2	-3.8	-8.9	-3.9	-3.9
b3lyp/6-311+g(d,p)	-3.9	-3.4	-3.4	-4.2	-4.2	-4.2	-4.2	-1.5	-1.2	-1.9	-1.6	-1.9	-1.6	-5.3	-0.5	-5.1	-0.6	-0.6
b3lyp/6-311++g(d)	-7.9	-6.7	-6.6	-7.5	-7.4	-7.5	-7.5	-4.7	-4.3	-5.1	-4.7	-5.1	-4.7	-8.9	-3.5	-8.6	-3.6	-3.6
b3lyp/6-311++g(d,p)	-3.4	-2.9	-2.9	-3.7	-3.7	-3.7	-3.7	-1.1	-0.7	-1.4	-1.1	-1.4	-1.1	-4.8	0.0	-4.6	-0.1	-0.1
b3lyp/cc-pVDZ	23.8	26.4	26.5	25.5	25.6	25.5	25.6	28.6	29.3	28.2	28.8	28.2	28.9	23.6	30.2	24.0	30.1	30.0
b3lyp/cc-pVTZ	-10.0	-6.6	-6.4	-7.5	-7.3	-7.6	-7.3	-4.3	-3.5	-4.7	-3.9	-4.7	-3.9	-9.7	-2.5	-9.1	-2.6	-2.7
b3lyp/aug-cc-pVDZ	-56.4	-56.8	-56.9	-57.7	-57.7	-57.7	-57.7	-54.9	-54.6	-55.3	-55.0	-55.3	-55.0	-58.6	-53.8	-58.5	-53.9	-53.9
b3lyp/aug-cc-pVTZ	-14.2	-12.9	-12.8	-13.8	-13.7	-13.8	-13.7	-10.8	-10.3	-11.2	-10.7	-11.2	-10.7	-15.3	-9.4	-15.0	-9.5	-9.6
b3lyp/aug-cc-pVTZ-J	-30.2	-27.7	-27.6	-28.8	-28.6	-28.8	-28.6	-25.3	-24.6	-25.7	-25.1	-25.7	-25.1	-30.7	-23.6	-30.3	-23.7	-23.8

Table 8S. Experimental, DFT-calculated, and differences between experimental and calculated $^1J_{CH}$ couplings for seven alkynes.

Compounds	J^{exp}, Hz[a]	J^{calc}, Hz[b]	ΔJ,[c] Hz
chloroacetylene	270.0	266.0	-4.0
bromoacetylene	261.0	261.9	0.9
iodoacetylene	255.0	257.2	2.2
acetylene	249.0	250.1	1.1
fluoroacetylene	277.7	280.1	2.4
phenylacetylene	251.0	248.8	-2.2
propylene	247.6	247.2	-0.4

[a] Experimental *J*-couplings from ref. 8.

[b] *J*-couplings were calculated at the B3LYP/6-311G(d,p)//B3LYP/6-311G(d,p) level of theory using *spinspin* method. RMSD was 2.2 Hz (0.8%).

[c] $\Delta J = J^{calc} - J^{exp}$.

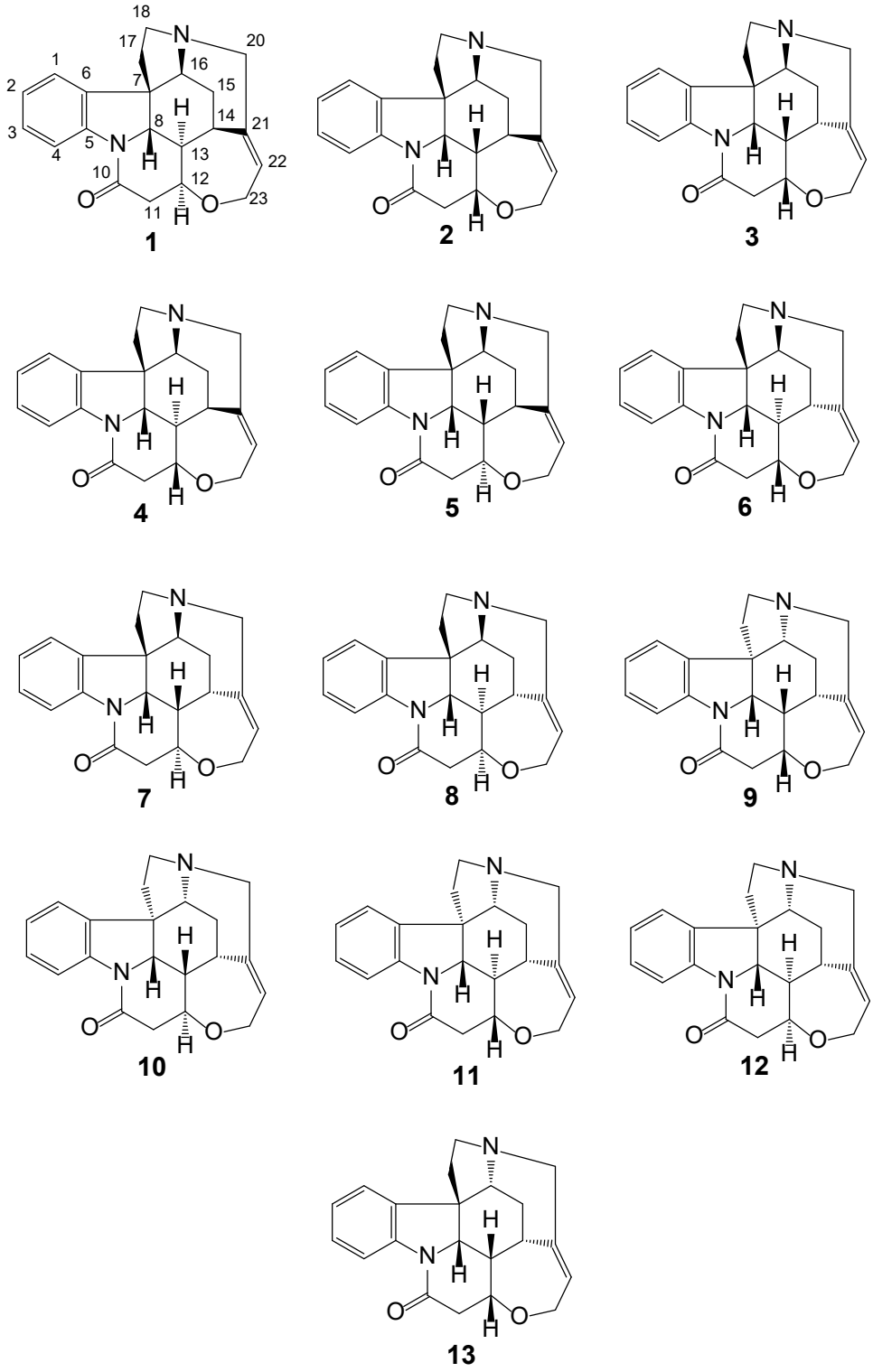
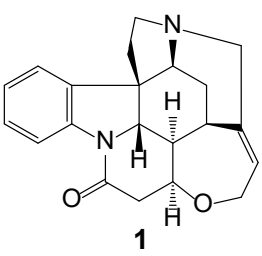


Figure 7S. Thirteen energetically feasible diastereomers of strychnine.[9]

Table 9S. $^{1}J_{CH}$ Couplings, RMSD and maximum *J*-coupling deviations (max_d) for possible conformations (**1a**-**1c**) and diastereomers (**2**-**13**) of strychnine[a]



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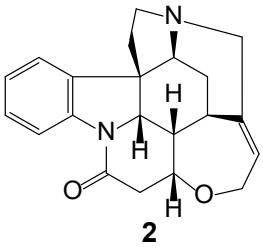
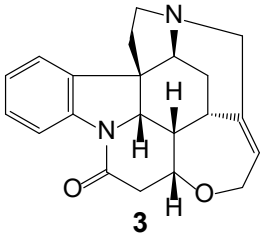


2



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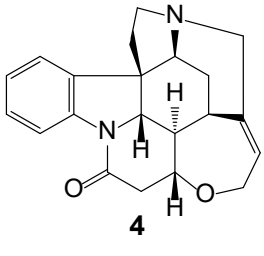

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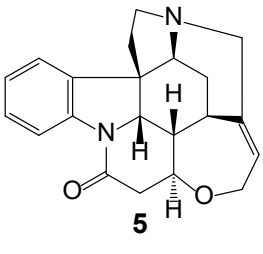
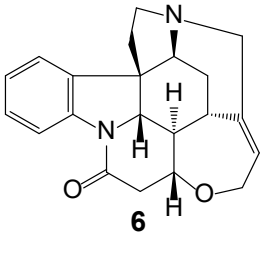
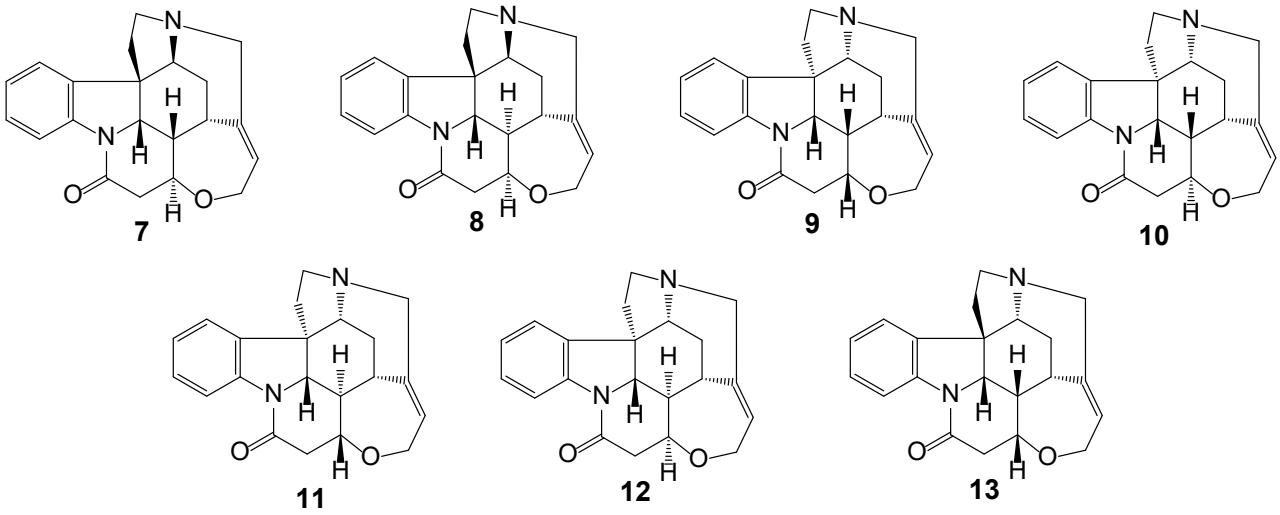


5



6

Proton	Exp.	**1a**	**1b**	**1c**	**2**	**3**	**4**	**5**	**6**
H1	158.36	157.1	156.3	157.5	157.4	157.9	157.4	157.3	158.3
H11a	134.16	137.9	134.7	141.9	135.9	140.1	134.5	140.9	139.5
H11b	124.74	126.3	128.0	123.3	127.8	122.5	131.0	126.3	121.9
H12	149.12	145.8	145.8	151.4	143.8	141.7	142.0	144.0	148.9
H13	124.2	125.6	127.1	128.0	132.2	128.6	131.4	131.4	131.0
H14	129.82	130.2	131.3	137.3	139.1	140.6	137.1	134.0	140.7
H15a	130.96	131.2	131.9	131.2	132.5	139.8	130.8	131.7	139.6
H15b	129.94	130.8	130.6	130.6	130.1	139.0	130.2	130.8	138.8
H16	146.36	147.5	147.3	146.6	151.1	157.1	147.1	149.9	153.4
H17a/b	134.12	132.2	133.8	132.4	130.3	138.1	132.5	131.0	138.3
H17b/a	134.12	136.1	130.7	135.7	133.7	136.2	136.1	136.0	137.0
H18a	145.92	145.8	140.4	146.3	144.9	148.9	146.3	145.7	149.7
H18b	130.24	130.5	135.9	129.9	129.7	135.2	129.6	130.0	136.1
H2	159.8	160.7	160.5	160.7	160.7	160.3	160.7	161.0	160.5
H20a	138.16	138.5	139.7	139.9	140.3	151.5	136.7	139.8	153.5
H20b	137.86	137.8	135.3	137.8	137.6	136.4	138.6	137.5	139.9
H22	158.4	159.6	158.7	151.5	154.4	160.3	153.6	161.6	160.1
H23a	136.64	134.9	135.1	135.2	137.0	135.9	141.6	138.5	139.2
H23b	144.42	144.7	144.7	144.9	146.1	146.1	144.7	147.1	147.1
H3	158.6	159.3	159.3	159.6	159.7	159.3	159.5	159.6	159.6
H4	168.26	172.9	172.7	172.1	172.9	173.8	172.2	171.9	173.0
H8	144.94	145.0	147.7	144.6	141.0	153.8	141.0	141.0	153.0
RMSD, Hz		1.77	2.64	3.12	3.66	6.23	3.60	3.22	6.12
max_d, Hz		4.60	5.47	7.21	7.57	12.75	14.86	7.98	13.70



Proton	Exp.	7	8	9	10	11	12	13
H1	158.36	158.2	158.7	158.5	158.6	158.5	158.4	155.0
H11a	134.16	138.3	143.0	137.9	137.6	137.3	140.1	140.1
H11b	124.74	130.6	130.2	122.6	128.7	126.3	123.9	124.7
H12	149.12	140.5	145.7	140.5	140.0	142.5	143.4	144.4
H13	124.2	134.7	128.0	121.8	131.0	132.2	134.7	123.9
H14	129.82	147.8	149.0	130.9	136.3	132.2	140.7	132.3
H15a	130.96	139.2	139.2	132.3	131.5	131.5	131.8	132.9
H15b	129.94	139.2	139.0	130.2	130.1	130.2	129.7	133.0
H16	146.36	154.0	152.8	149.0	148.9	150.4	150.7	144.3
H17a/b	134.12	138.1	137.5	136.6	129.6	133.6	133.2	143.7
H17b/a	134.12	136.6	137.3	134.2	136.4	133.5	133.2	135.0
H18a	145.92	148.8	149.7	139.2	139.2	143.9	144.2	147.2
H18b	130.24	135.4	136.6	137.0	137.9	131.7	131.0	139.2
H2	159.8	160.5	160.7	160.0	160.2	160.4	160.5	159.6
H20a	138.16	150.9	155.1	139.1	139.3	139.4	140.2	141.0
H20b	137.86	136.8	145.4	138.7	136.8	139.2	138.7	137.3
H22	158.4	153.3	154.6	157.1	151.7	161.4	155.1	160.9
H23a	136.64	141.2	140.9	135.6	141.1	136.7	139.5	134.5
H23b	144.42	144.6	148.5	145.0	144.3	145.9	146.2	146.2
H3	158.6	159.5	159.6	159.7	159.9	159.9	159.9	160.1
H4	168.26	172.7	170.9	170.9	170.7	171.1	170.1	169.8
H8	144.94	155.7	152.7	134.8	137.6	138.0	137.4	147.1
RMSD, Hz		7.31	7.47	3.82	4.59	3.18	4.33	3.67
max_d, Hz		8.71	8.69	18.05	9.13	9.70	8.50	10.86

[a] *J*-Couplings were calculated at the B3LYP/6-31G(d,p)(mixed)//mPW1PW/cc-pVTZ level of theory.

Experimental details for *ent*-Trachyloban-6β,18,19-trihydroxy-2-one (14)

General experimental procedures

Optical rotations were measured on a Rudolph Research Analytical Autopol IV polarimeter equipped with a sodium lamp (589 nm) and a 1 dm microcell. NMR experiments were performed on a Bruker DRX-600 spectrometer (Bruker BioSpin GmBH, Rheinstetten, Germany) equipped with a Bruker 5 mm TCI CryoProbe at 300 K. All 2D NMR spectra were acquired in methanol-d_4 (99.95%, Sigma-Aldrich), standard pulse sequences and phase cycling were used for DQF-COSY, HSQC, and HMBC spectra. HRESIMS spectra were acquired in the positive ion mode on a XL Orbitrap™ instrument (Thermo-Fisher). TLCs were performed on precoated Kieselgel 60 F_{254} plates (Merck AG), and compounds were detected by spraying with a $Ce(SO_4)_2/H_2SO_4$ solution. Column chromatography was performed over silica gel (70–220 mesh, Merck). Reversed-phase (RP) HPLC separations were conducted using a Shimadzu LC-20AT series pumping system equipped with a Shimadzu RID10A refractive index detector and a Shimadzu injector, using a C_{18} μ-Bondapak™ column (30 cm x 7.8 mm, 10 μm, Waters–Milford) and a mobile phase consisting of MeOH-H_2O mixtures at a flow rate of 2.5ml/min.

Plant material

Leaves of *Psiadia punctulata* (DC.) Vatke (Asteraceae) were collected in Wadi Ghazal, Saudi Arabia, in June 2012 near Wadi Thee Ghazal about 25 km south of Taif City, Saudi Arabia (Coordinates: 21° 08’ N 40° 22’ E). The plant material was identified morphologically by Prof. Ammar Bader. A voucher specimen (SA/IT 2013/1) was deposited in the Laboratory of Pharmacognosy at *Umm Al-Qura University,* Saudi Arabia.

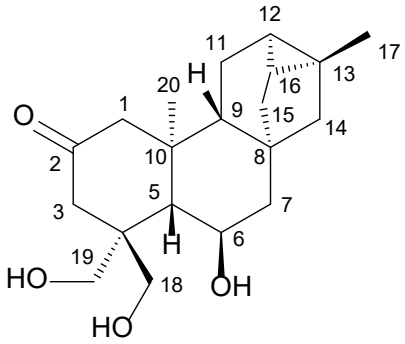
Extraction and isolation

The exudate of *P. punctulata* (10.0 g) was obtained by dipping 201 g of fresh leaves into 2.1 L of dichloromethane for less than 30 sec, after which the leaves were dried at 40 °C. The exudate was dissolved in chloroform and separated on silica gel column, eluted with step gradients of $CHCl_3$-MeOH (100:0, 90:10, 80:20, 70:30, 50:50 and 0:100). Fractions of 50 mL were collected, analysed by TLC and grouped into nine main fractions (A-I). Fraction B (322.0 mg) and was subjected to semi-preparative reversed phase HPLC (MeOH-H_2O, 65:35) to yield compound **14** (50.0 mg, t_R 11 min).

ent-Trachyloban-6β,18,19-trihydroxy-2-one (**14**)

White substance; $[\alpha]_D^{25}$: -129° (c 0.26, CH_3OH); ^1H NMR (CD_3OD, 600 MHz) and ^{13}C NMR (CD_3OD, 150 MHz), see Table 6S ; HRESIMS *m/z* 335.2216 $[M+H]^+$, calcd. for $C_{20}H_{30}O_3$, 335.2211.

Table 10S. ^1H and ^{13}C NMR data of compound **14** (CD_3OD, 600 MHz, δ in ppm and *J* in Hz in parenthesis)



14

Position	δ_c	δ_H	HMBC[b]
1	53.0	1.93[a]; 2.21 d (16.0)	2, 5, 9, 10, 20
2	213.4	-	-
3	45.7	2.35[a]; 2.41 d (16.3)	2, 4, 5, 18, 19
4	44.7	-	-
5	54.4	1.59, d (11.0)	6, 9, 10, 20, 18,19
6	67.0	3.95, br dd (5.0,11.0)	-
7	48.5	1.73, dd (5.0,12.0), 1.39 [a]	5, 6, 8
8	41.8	-	-
9	52.5	1.40[a]	11, 20
10	43.0	-	-
11	20.7	1.69[a]; 1.96 m	10, 12
12	20.0	0.66 br d (7.4)	-
13	25.0	0.90 dd (7.7, 2.5)	12, 14, 8
14	34.2	1.34 br d (11.7); 2.09 , dd (11.8, 2.5)	12
15	52.1	1.35[a]; 1.48[a]	78, 9, 14, 16, 17
16	22.7	-	-
17	20.7	1.16 s	12, 13, 15
18	31.4	3.72, d (11.0); .3.52, d (11.0)	3, 4, 5, 19
19	68.0	3.65 d (10.9); 3.95 d (10.9)	3, 4, 5, 18
20	17.4	1.13 s	1, 9, 10

[a]Overlapped signal. [b]·HMBC correlations are from proton(s) stated to the indicate carbon(s). Assignments were confirmed by COSY, 1D-TOCSY and HSQC experiments.

Measurements of $^{1}J_{CH}$ couplings in **14**

$^{1}J_{CH}$ Couplings for **14** were measured in DMSO-d_6 on a Bruker 600 MHz spectrometer equipped with a 1.7 mm TXI MicroCryoProbe™ using a *J*-resolved F1-iINEPT HSQC pulse sequence with $^{1}J_{CH}$ optimized to 145 Hz. Four scans were accumulated for each of the 512 t_1 increments with the number of data points in t_2 set to 2048. The spectral window was 2705 Hz in F2 and 400 Hz (*J*-resolved) in F1 giving a FID resolution of 2.6 and 1.5 Hz, respectively. The recycle delay was set to 3 s, giving an overall experimental time of 2 h 8 min. Prior to Fourier-transformation, the data set was zero-filled to 4096 in F2, 2048 in F1; a π/2-shifted sine-squared window function was applied in both dimensions.

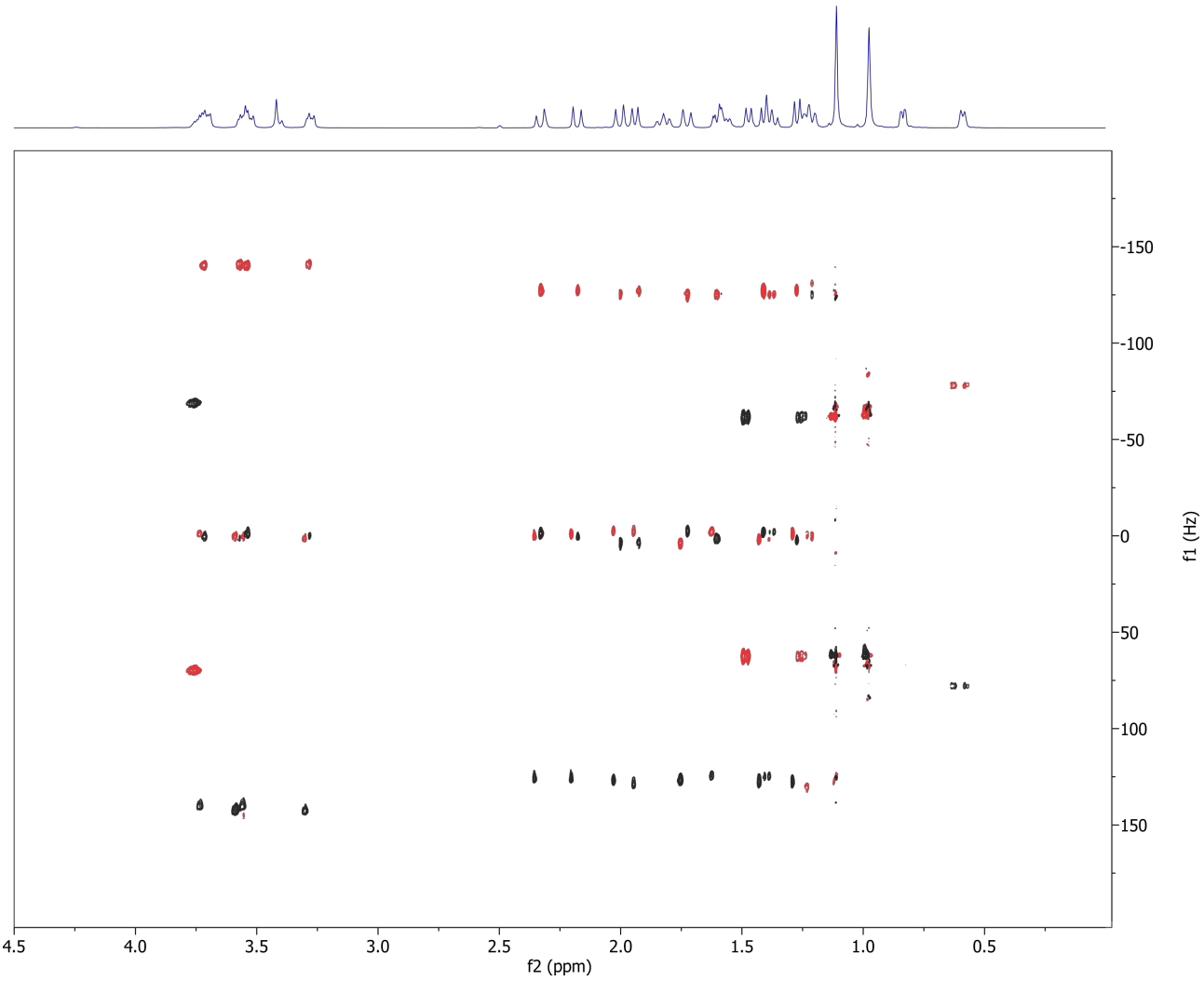


Figure 8S. *J*-resolved F1-iINEPT HSQC spectrum of **14** in DMSO-d_6 at 25 °C

Stereochemical analysis of **14**

Relative stereochemistry in **14** was determined using ROESY data as shown in Figure 8S below. The ROESY spectrum of **14** was acquired in DMSO-d_6 on a Bruker 600 MHz spectrometer equipped with a 1.7 mm TXI MicroCryoProbe™. Eight scans were accumulated for each of the 512 t_1 increments with the number of data points in t_2 set to 4096. Spectral window was 3597.1 Hz in F2 and F1 dimensions, respectively. The mixing time was set to 400 ms, the recycle delay was set to 1.5 s, giving an overall experimental time of 2 h 51 min. Prior to Fourier-transformation, the data set was zero-filled to 4096 points in F2 and 2048 points in F1; a π/2-shifted sine-squared window function was applied in both dimensions.

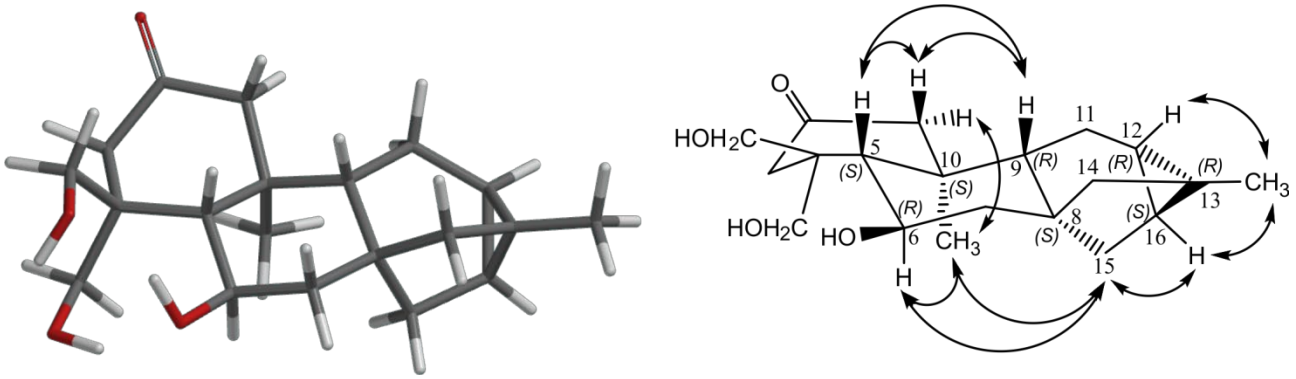


Figure 9S. Left: lowest energy conformation of **14**. Right: ChemDraw structure of **14** with the most relevant ROE correlations represented by double-headed arrows.

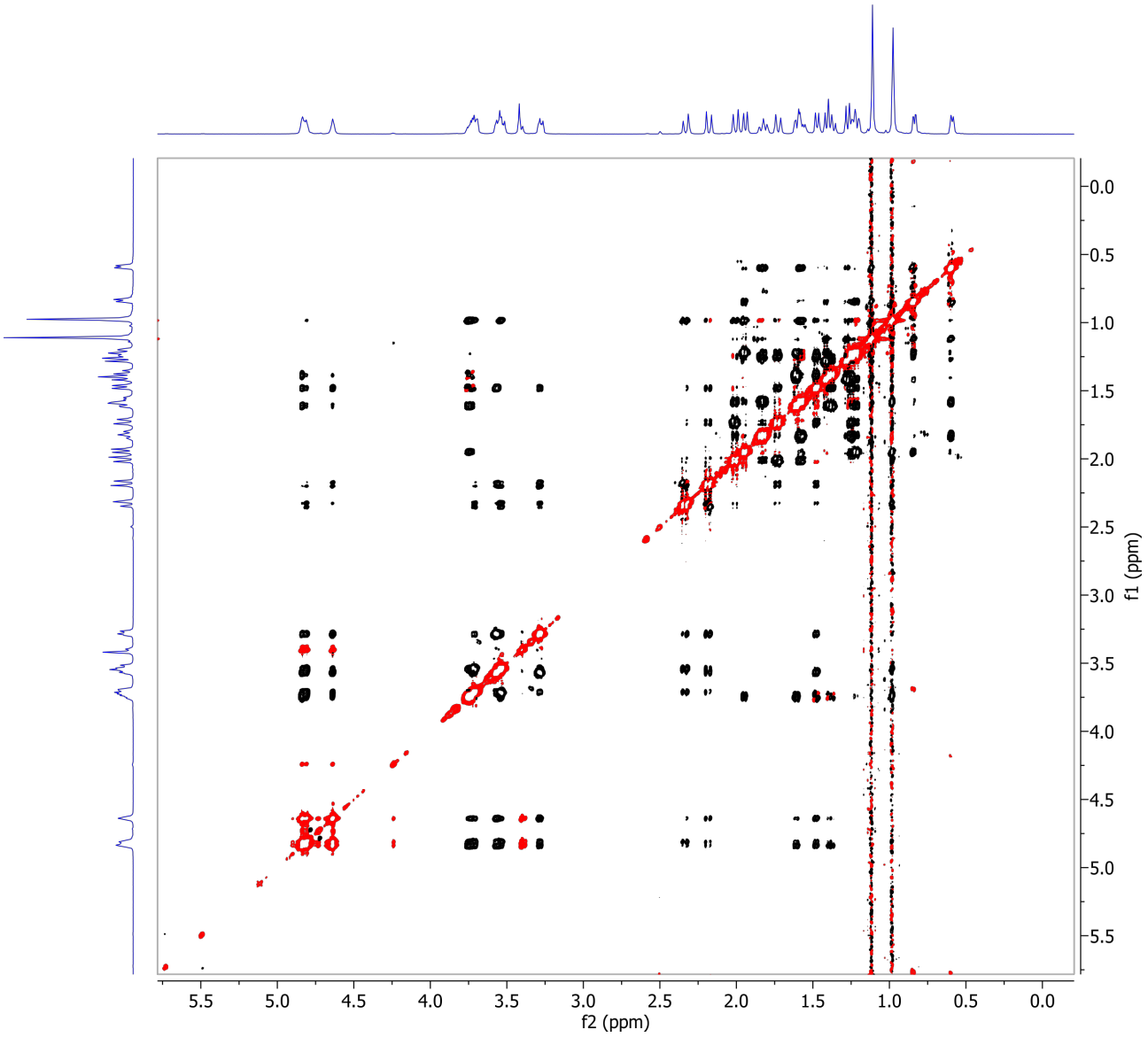


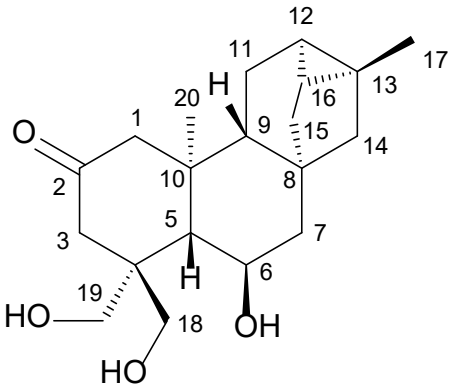
Figure 10S. ROESY spectrum of **14** in DMSO-d_6 at 25 °C

Table 11S. RMSD, max_d, correlation coefficients *R* and number of analyzed conformations for diterpene **14** and its isomers **15**-**19**.

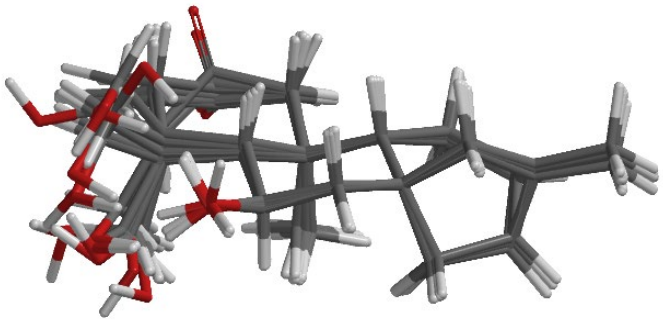
	Structures					
	14	**15**	**16**	**17**	**18**	**19**
RMSD, Hz	2.03	3.86	2.68	2.62	2.69	2.19
max_d, Hz	3.78	11.32	6.42	5.79	5.86	4.24
R	0.9972	0.9596	0.9860	0.9851	0.9886	0.9954
# of conf[a]	111(9)	72(5)	146(11)	207(4)	125(8)	117(10)

[a] Number of conformations generated by Spartan'16 program[1] using MMFF force filed with 10 kcal/mol cutoff energy. These ensembles of conformations were subsequently optimized at the B3LYP/6-31+G(d,p) level using Gaussian16 program.[4] The number in parenthesis is the final number of conformations with weights >1% which were used for *J*-coupling analysis at the B3LYP/6-31G(d,p)//mPW1PW/cc-pVTZ model chemistry and "mixed" method[6] using Gaussian16 program.

Table 12S. $^{1}J_{CH}$ Couplings for the nine lowest energy conformations of **14**, conformational weights, averaged $^{1}J_{CH}$ couplings, RMSD and maximum *J*-coupling deviation (max_d) for **14**

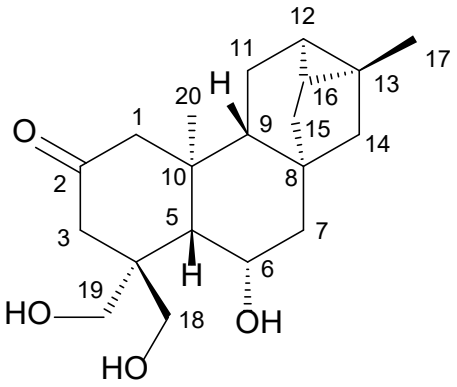


14

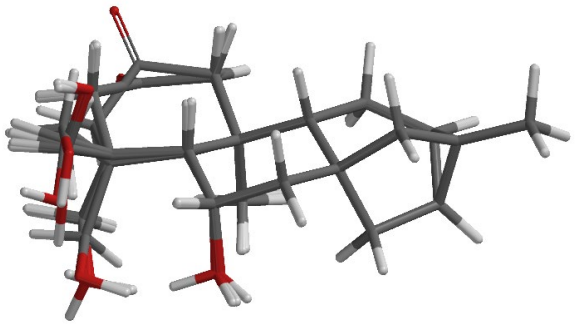


Proton	Exp.	14-1	14-2	14-3	14-4	14-5	14-6	14-7	14-8	14-9	Averaged
H1b	124.1	125.7	126.3	124.5	123.0	123.5	130.4	123.3	124.4	124.4	125.4
H1a	129.4	129.7	129.1	136.3	136.5	136.1	125.0	136.1	136.9	136.3	132.0
H3a	128.6	134.0	134.8	128.0	123.4	120.7	138.9	120.7	119.2	123.7	130.3
H3b	126.0	123.2	122.3	134.1	135.8	140.9	122.6	140.9	136.3	138.6	128.6
H5	124.5	123.7	124.5	125.8	122.8	124.8	123.9	122.6	124.0	125.5	124.2
H6	139.1	141.4	137.8	142.2	149.3	141.8	135.7	145.2	141.5	135.8	141.1
H7b	123.2	125.0	125.4	125.3	126.3	127.2	125.3	120.5	125.0	125.8	125.1
H7a	127.1	132.3	131.9	131.1	124.8	125.2	131.4	131.4	132.6	131.5	131.0
H9	125.7	125.9	126.0	126.6	125.9	126.2	126.6	125.8	125.7	126.3	126.1
H11b	124.2	124.8	124.7	125.1	126.0	125.9	124.8	125.9	125.0	125.0	125.1
H11a	127.1	129.2	129.1	128.8	129.0	129.4	128.6	129.3	129.2	128.7	129.1
H12	156.1	158.0	157.9	158.0	158.2	158.6	157.7	158.6	158.5	157.8	158.1
H14b	126.2	128.1	128.1	127.8	127.3	127.3	128.1	127.5	128.1	128.1	127.9
H14a	130.1	131.7	131.8	131.7	131.9	132.2	131.7	131.8	131.6	131.7	131.8
H15b	125.8	128.5	128.6	128.2	127.4	127.6	128.5	128.2	129.0	128.5	128.4
H15a	130.4	131.8	131.6	132.0	133.8	132.7	131.5	132.8	131.4	131.9	132.0
H16	165.3	168.5	168.5	168.1	168.7	169.0	168.1	169.1	168.9	167.9	168.5
H18b	141.6	142.5	143.7	141.5	144.6	147.1	140.6	147.6	143.1	146.2	143.3
H18a	142.8	145.4	143.5	141.6	139.2	140.1	152.2	137.4	146.2	147.2	143.8
H19b	140.0	139.8	144.8	146.1	145.1	138.1	144.3	138.2	141.4	143.7	142.2
H19a	141.2	144.5	143.6	137.5	137.8	143.9	145.8	144.4	144.3	143.1	142.8
Met17	124.4	126.4	126.4	126.3	126.4	126.5	126.3	126.5	126.4	126.3	126.4
Met20	124.9	126.6	126.5	127.2	128.4	127.6	126.3	127.8	127.4	127.3	127.0
Weights, %		35.3	18.0	15.2	6.5	6.4	5.8	5.7	3.7	3.4	
RMSD, Hz											2.03
max_d, Hz											3.89

Table 13S. $^{1}J_{CH}$ Couplings for the five lowest energy conformations of **15**, conformational weights, averaged $^{1}J_{CH}$ couplings, RMSD and maximum *J*-coupling deviation (max_d) for **15**

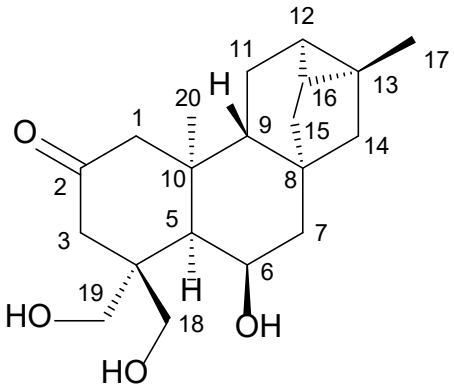


15

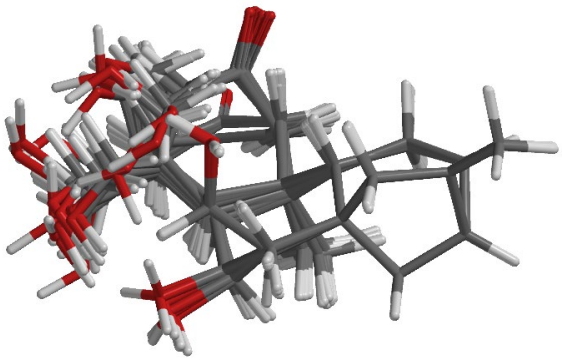


Proton	Exp.	15-1	15-2	15-3	15-4	15-5	Averaged
H1b	124.1	122.9	122.8	123.0	128.2	123.7	123.0
H1a	129.4	136.7	137.0	136.1	126.8	136.2	136.6
H3a	128.6	135.9	135.0	134.2	122.2	132.9	123.4
H3b	126.0	123.0	123.1	126.3	134.7	129.4	135.6
H5	124.5	118.2	117.4	121.5	120.5	121.5	118.3
H6	139.1	151.2	142.5	144.0	151.4	139.1	150.4
H7b	123.2	123.0	120.5	124.1	124.6	121.8	125.9
H7a	127.1	125.6	130.9	124.9	124.5	130.4	122.9
H9	125.7	125.3	124.5	125.7	125.9	125.4	125.2
H11b	124.2	126.0	125.3	126.1	125.7	125.2	125.9
H11a	127.1	128.6	127.8	128.5	128.8	127.9	128.5
H12	156.1	158.0	157.3	157.9	158.0	157.1	158.0
H14b	126.2	127.2	127.5	126.9	127.2	127.4	127.2
H14a	130.1	131.4	130.3	131.5	131.9	130.7	131.3
H15b	125.8	126.6	129.5	126.0	125.6	129.1	135.9
H15a	130.4	135.9	136.9	136.1	135.0	136.4	126.7
H16	165.3	168.2	167.2	168.1	168.3	166.9	168.1
H18b	141.6	142.7	139.7	141.5	143.4	140.7	142.5
H18a	142.8	143.4	147.9	141.5	142.3	145.7	143.6
H19b	140.0	140.5	140.8	146.7	139.9	145.0	142.1
H19a	141.2	142.1	143.0	139.1	144.1	138.5	140.7
Met17	124.4	126.3	126.0	126.3	126.4	126.0	126.3
Met20	124.9	128.1	128.1	127.9	127.0	127.6	128.0
Weights, %		89.2	5.1	3.1	1.6	1.0	
RMSD, Hz							3.86
max_d, Hz							11.32

Table 14S. $^{1}J_{CH}$ Couplings for the eleven lowest energy conformations of **16**, conformational weights, averaged $^{1}J_{CH}$ couplings, RMSD and maximum *J*-coupling deviation (max_d) for **16**

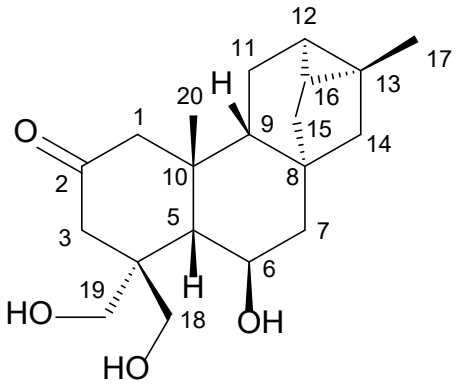


16

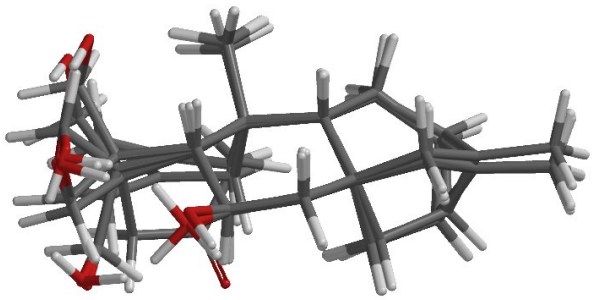


Proton	Exp.	**16-1**	**16-2**	**16-3**	**16-4**	**16-5**	**16-6**	**16-7**	**16-8**	**16-9**	**16-10**	**16-11**	**Averaged**
H1b	124.1	122.6	137.1	137.3	134.7	122.1	122.3	134.0	123.7	122.7	136.5	136.2	129.1
H1a	129.4	133.7	124.9	124.7	122.6	134.4	133.9	124.5	137.2	134.2	123.1	124.1	129.5
H3a	128.6	133.4	135.8	136.2	124.4	129.4	137.8	125.0	124.8	132.5	137.0	141.7	132.7
H3b	126.0	122.8	122.5	121.2	129.7	123.5	121.6	129.7	131.2	123.5	124.6	122.8	123.9
H5	124.5	122.2	125.8	125.1	128.8	120.2	120.9	132.7	124.5	121.4	125.3	126.3	124.3
H6	139.1	153.3	143.5	142.8	138.9	138.1	144.8	139.3	137.6	143.6	140.8	139.7	145.5
H7b	123.2	124.4	129.2	130.3	130.9	121.6	124.4	125.7	123.6	121.3	121.9	124.3	126.3
H7a	127.1	126.2	126.5	125.1	125.4	131.5	126.1	127.2	134.8	131.0	135.4	128.1	127.1
H9	125.7	129.8	124.6	124.7	123.6	130.8	129.1	123.9	128.0	132.1	125.6	126.0	127.2
H11b	124.2	125.0	124.3	124.3	125.3	124.1	125.3	125.7	125.5	123.9	124.6	124.6	124.8
H11a	127.1	129.7	132.0	132.1	130.3	129.0	130.1	130.5	128.6	128.8	131.0	132.3	130.5
H12	156.1	158.8	158.4	158.3	158.5	158.1	159.0	158.5	157.9	157.7	158.4	158.6	158.5
H14b	126.2	126.1	127.8	127.8	127.6	126.5	125.9	127.2	127.1	126.3	127.5	127.0	126.9
H14a	130.1	132.8	132.1	132.2	131.7	137.6	132.9	131.9	134.1	137.7	133.7	133.3	132.9
H15b	125.8	128.2	128.7	128.8	128.7	128.2	128.1	127.6	127.5	128.0	128.1	127.8	128.3
H15a	130.4	132.5	131.1	131.1	131.0	131.4	132.9	131.6	131.2	131.0	130.3	131.2	131.7
H16	165.3	169.8	168.9	168.9	169.1	168.9	170.2	169.1	168.4	168.4	169.0	169.1	169.3
H18b	141.6	138.7	143.7	142.2	140.2	141.6	142.0	139.3	144.1	139.7	144.4	146.5	141.1
H18a	142.8	142.9	143.8	146.5	142.3	146.1	138.7	141.7	142.4	144.3	140.7	140.2	143.3
H19b	140.0	138.9	144.5	141.3	139.7	145.2	139.3	138.9	141.4	145.0	142.9	141.2	141.2
H19a	141.2	143.0	143.1	144.9	143.5	142.0	144.7	143.1	138.2	141.1	140.8	143.9	143.0
Met17	124.4	126.4	126.4	126.4	126.5	126.2	126.5	126.5	126.3	126.1	126.4	126.5	126.4
Met20	124.9	127.0	127.4	127.4	127.1	127.0	127.1	127.1	127.6	126.6	127.2	127.1	127.2
Weights, %		33.8	21.2	10.6	7.8	6.7	5.7	5.4	4.8	1.6	1.3	1.1	
RMSD, Hz													2.68
max_d, Hz													6.42

Table 15S. $^{1}J_{CH}$ Couplings for the four lowest energy conformations of **17**, conformational weights, averaged $^{1}J_{CH}$ couplings, RMSD and maximum *J*-coupling deviation (max_d) for **17**

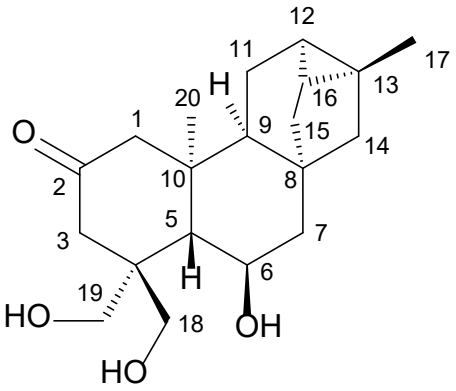


17

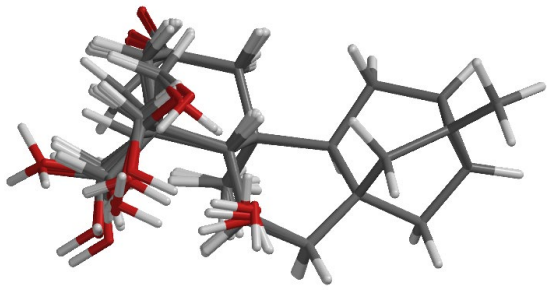


Proton	Exp.	**17-1**	**17-2**	**17-3**	**17-4**	**Averaged**
H1b	124.1	121.8	121.8	121.6	134.9	122.0
H1a	129.4	135.7	134.9	134.9	120.9	135.2
H3a	128.6	134.2	124.6	125.6	123.3	130.3
H3b	126.0	120.6	131.9	131.5	131.2	125.2
H5	124.5	132.0	127.1	128.2	131.8	130.2
H6	139.1	139.1	139.5	136.1	138.4	138.8
H7b	123.2	126.9	126.0	126.0	126.8	126.5
H7a	127.1	124.7	132.5	132.2	125.5	127.8
H9	125.7	126.4	126.3	126.3	126.8	126.3
H11b	124.2	126.4	126.0	125.9	126.6	126.2
H11a	127.1	129.8	128.9	128.9	128.8	129.4
H12	156.1	158.5	158.2	158.1	158.0	158.3
H14b	126.2	127.0	128.3	128.3	127.5	127.5
H14a	130.1	132.4	131.4	131.3	131.2	132.0
H15b	125.8	127.6	128.8	128.8	126.6	128.1
H15a	130.4	131.2	130.4	130.2	135.9	130.9
H16	165.3	169.1	168.7	168.5	168.8	168.9
H18b	141.6	143.7	138.0	142.7	145.1	142.0
H18a	142.8	142.8	145.7	144.7	142.1	143.8
H19b	140.0	138.2	140.6	142.2	139.5	139.4
H19a	141.2	145.5	145.9	144.4	141.7	145.4
Met17	124.4	126.5	126.4	126.4	126.3	126.4
Met20	124.9	128.7	127.1	127.0	128.7	128.1
Weights, %		58.0	26.6	14.1	1.2	
RMSD, Hz						2.62
max_d, Hz						5.79

Table 16S. $^{1}J_{CH}$ Couplings for the eight lowest energy conformations of **18**, conformational weights, averaged $^{1}J_{CH}$ couplings, RMSD and maximum *J*-coupling deviation (max_d) for **18**

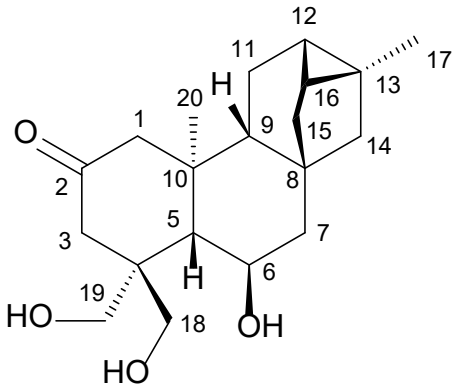


18

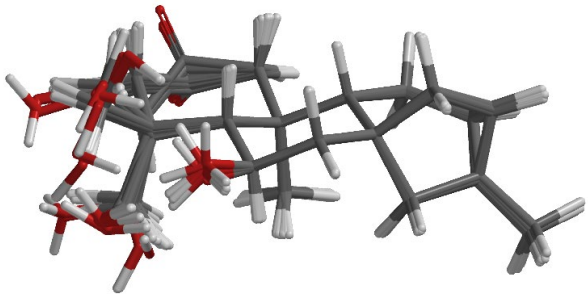


Proton	Exp.	18-1	18-2	18-3	18-4	18-5	18-6	18-7	18-8	Averaged
H1b	124.1	122.2	124.0	124.6	124.7	123.9	122.2	124.5	123.6	123.3
H1a	129.4	134.7	135.8	135.5	135.9	135.6	134.5	135.7	135.2	135.3
H3a	128.6	124.0	135.9	138.2	132.6	140.1	123.5	135.1	133.6	130.4
H3b	126.0	130.9	123.3	124.4	125.8	122.1	131.6	126.5	129.8	127.2
H5	124.5	124.1	123.4	126.0	126.0	124.7	124.3	125.0	123.5	124.2
H6	139.1	143.0	151.7	135.6	136.0	142.7	139.1	142.9	149.9	144.3
H7b	123.2	122.7	125.2	122.2	122.5	124.8	122.5	122.3	123.2	123.5
H7a	127.1	131.8	124.4	131.8	131.9	124.4	131.7	131.6	126.2	129.1
H9	125.7	128.8	128.9	128.4	128.6	128.8	128.7	128.4	128.5	128.8
H11b	124.2	124.6	124.4	124.0	123.8	124.7	124.4	123.8	124.8	124.4
H11a	127.1	131.0	131.7	130.9	130.9	131.8	130.9	130.8	131.3	131.3
H12	156.1	159.7	159.8	159.2	159.2	159.9	159.5	159.1	159.5	159.6
H14b	126.2	130.3	128.5	131.7	131.7	128.1	131.1	132.2	129.6	129.9
H14a	130.1	129.3	132.9	131.6	131.4	132.9	129.8	132.5	133.2	131.0
H15b	125.8	128.0	127.1	127.9	128.0	127.0	128.0	127.9	127.0	127.7
H15a	130.4	133.8	134.3	133.3	133.4	134.3	133.5	133.2	133.8	133.9
H16	165.3	167.7	167.6	166.8	166.9	167.8	167.4	166.6	167.0	167.5
H18b	141.6	144.5	138.9	142.0	142.4	143.7	143.0	139.4	136.3	142.2
H18a	142.8	140.3	144.3	143.7	146.0	138.3	144.9	145.6	144.0	142.4
H19b	140.0	143.7	140.1	145.7	145.9	139.7	142.8	146.2	142.3	142.7
H19a	141.2	141.6	144.2	146.7	143.7	147.7	143.7	141.9	142.1	143.4
Met17	124.4	126.5	126.4	126.2	126.2	126.4	126.4	126.1	126.2	126.4
Met20	124.9	126.7	127.6	126.8	126.9	127.2	126.6	126.9	127.1	127.0
Weights, %		41.9	30.0	8.5	7.8	5.2	5.0	0.8	0.7	
RMSD, Hz										2.69
max_d, Hz										5.86

Table 17S. $^{1}J_{CH}$ Couplings for the ten lowest energy conformations of **19**, conformational weights, averaged $^{1}J_{CH}$ couplings, RMSD and maximum *J*-coupling deviation (max_d) for **19**



19



Proton	Exp.	19-1	19-2	19-3	19-4	19-5	19-6	19-7	19-8	19-9	19-10	Averaged
H1b	124.1	126.2	126.7	124.6	123.5	129.8	124.5	124.4	124.7	123.7	125.9	125.9
H1a	129.4	129.3	128.8	136.2	136.1	125.4	137.0	136.2	136.7	136.3	129.2	131.3
H3a	128.6	134.1	135.0	127.9	120.7	138.7	119.4	123.7	125.5	126.8	139.6	131.6
H3b	126.0	123.4	122.4	134.1	140.8	122.4	136.3	138.6	132.7	134.7	120.6	127.3
H5	124.5	123.8	124.6	125.9	124.8	123.9	124.0	125.4	125.3	124.8	124.4	124.5
H6	139.1	141.3	137.8	142.1	141.7	135.5	141.4	135.8	136.2	147.5	141.0	140.1
H7b	123.2	125.0	125.4	125.3	127.2	125.3	125.1	125.8	125.8	126.5	126.9	125.3
H7a	127.1	132.4	131.9	131.0	125.1	131.4	132.5	131.4	131.5	125.1	125.2	131.3
H9	125.7	126.3	126.4	126.8	126.4	126.6	126.1	126.5	126.5	126.6	126.5	126.5
H11b	124.2	124.8	124.7	125.1	125.9	124.7	125.1	124.9	124.8	126.0	125.5	124.9
H11a	127.1	129.1	129.1	128.8	129.4	128.7	129.2	128.7	128.6	129.0	129.5	129.0
H12	156.1	158.1	158.1	157.8	158.5	157.6	158.3	157.7	157.8	158.2	158.4	158.0
H14b	126.2	127.6	127.6	127.3	126.6	127.6	128.0	127.5	127.6	126.4	126.7	127.5
H14a	130.1	131.0	130.9	131.3	132.1	130.8	130.8	131.2	131.3	132.7	131.7	131.1
H15b	125.8	129.1	129.1	128.8	128.3	129.0	129.0	129.2	129.2	128.2	128.3	129.0
H15a	130.4	132.6	132.6	132.5	132.9	132.5	132.5	132.5	132.4	132.7	133.1	132.6
H16	165.3	169.3	169.2	168.7	169.4	168.7	168.9	168.7	168.7	169.3	169.6	169.1
H18b	141.6	139.8	144.7	146.1	138.1	144.3	141.6	143.7	146.2	147.3	138.0	142.4
H18a	142.8	144.5	143.6	137.5	143.9	145.9	144.2	143.0	143.4	137.9	147.3	143.1
H19b	140.0	142.5	143.7	141.6	147.1	140.5	143.1	146.2	143.8	140.5	142.1	142.9
H19a	141.2	145.5	143.6	141.6	140.1	152.1	146.1	147.2	147.3	143.4	145.6	144.6
Met17	124.4	126.4	126.3	126.2	126.5	126.2	126.4	126.2	126.2	126.4	126.5	126.3
Met20	124.9	126.6	126.4	127.2	127.6	126.3	127.4	127.3	127.5	128.0	126.6	126.8
Weights, %		38.3	19.7	15.7	6.5	6.3	3.8	3.4	3.2	1.1	1.0	
RMSD, Hz												2.19
max_d, Hz												4.24

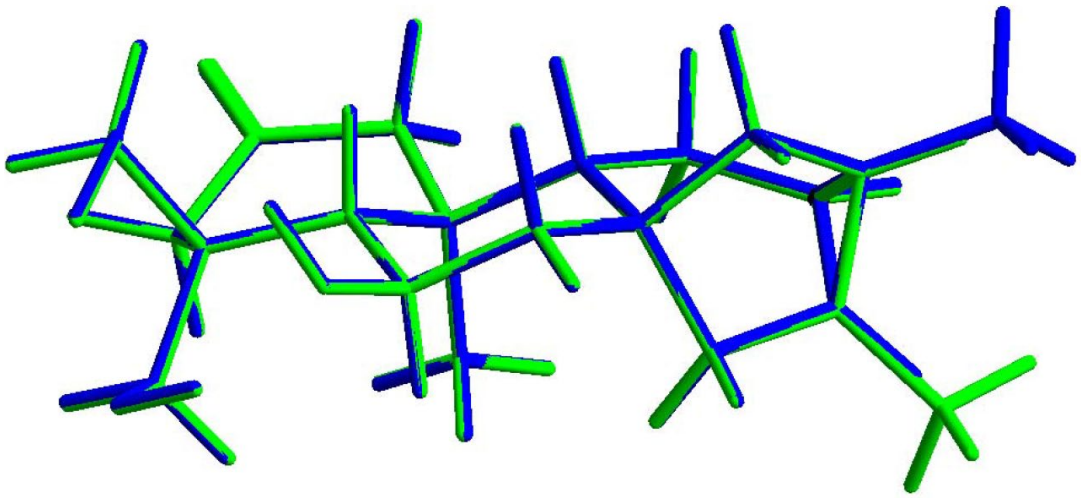


Figure 11S. Overlay of minimum energy conformations of **14** (blue) and **19** (green).

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