Supporting Information for

Effect of Protonation on the Confirmation of Cinchonidine

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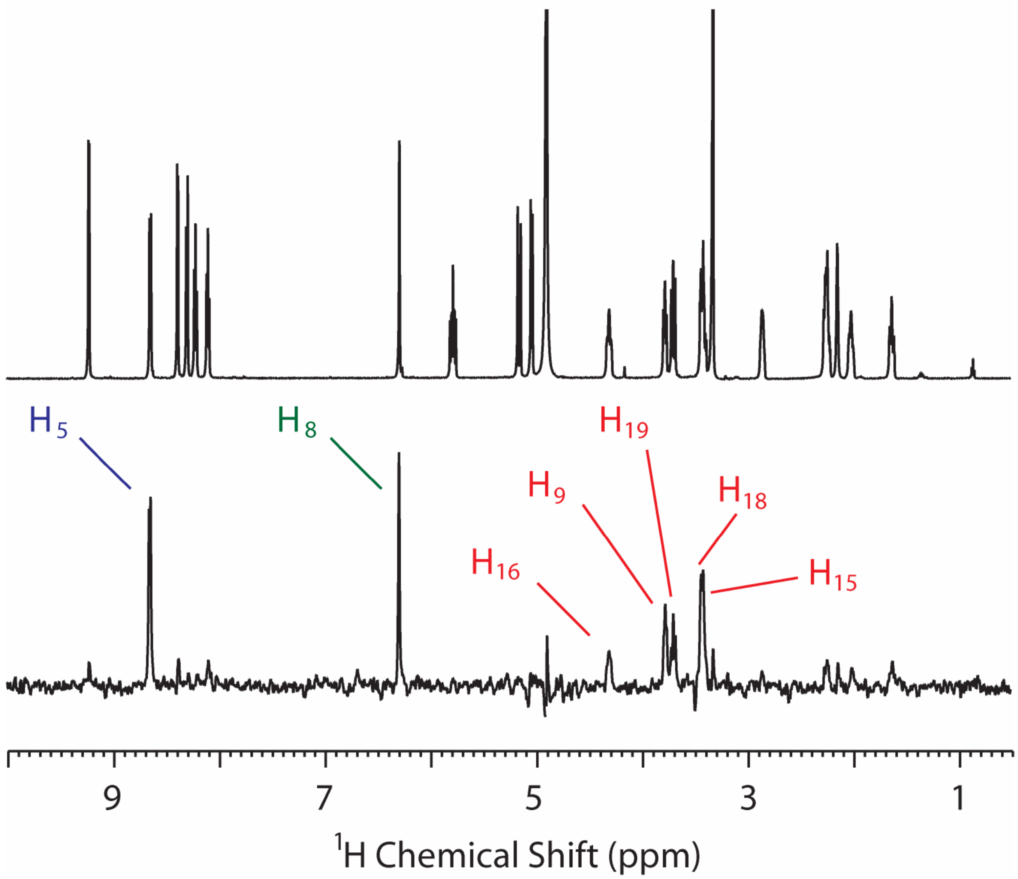
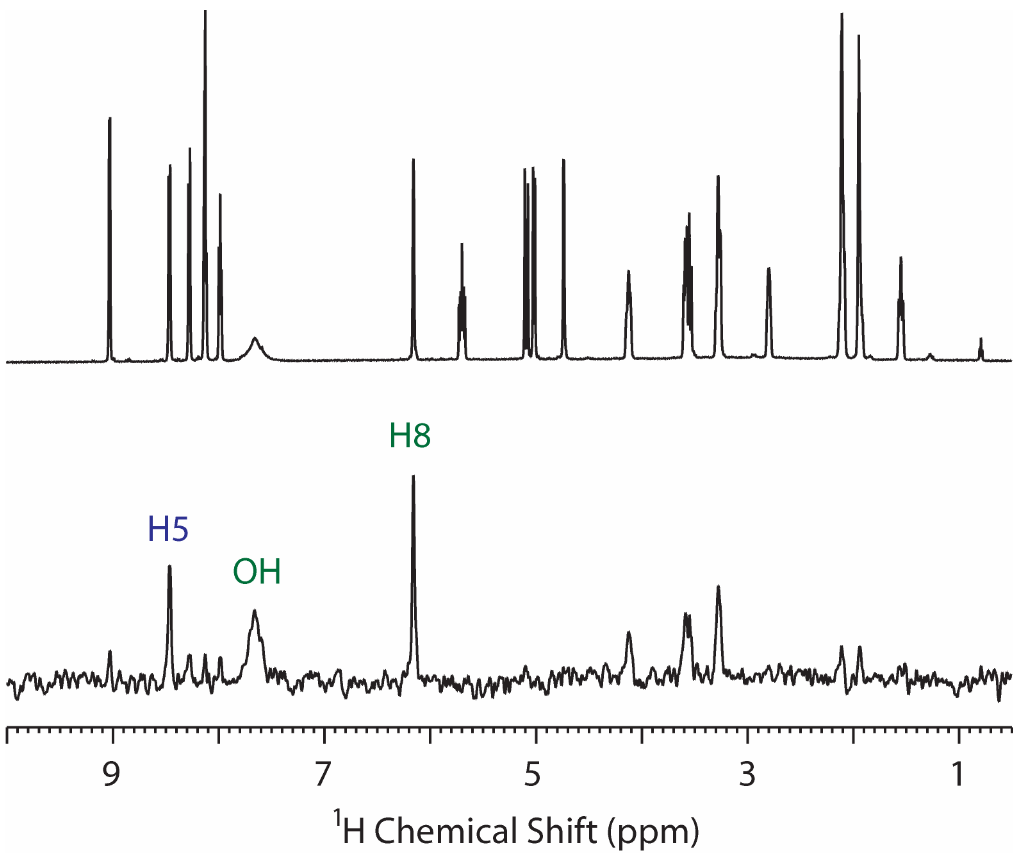
$^1H\{^{19}F\}$ NOE Difference Experiment in CD_3OD:

1D $^1H\{^{19}F\}$ NOE Difference Experiment of Cinchonidine·HF in deuterated methanol (bottom). Data were acquired on a 14.1 T Bruker Avance Spectrometer (^1H frequency 600.14 MHz) equipped with a double-resonance single-axis gradient proton-fluorine probe. 16k complex data points were acquired with a spectral width of 10.8 kHz. 2k scans were acquired with a mixing time of 250 ms and a relaxation delay of 1.5 s. For reference, the full 1D spectrum is shown above.



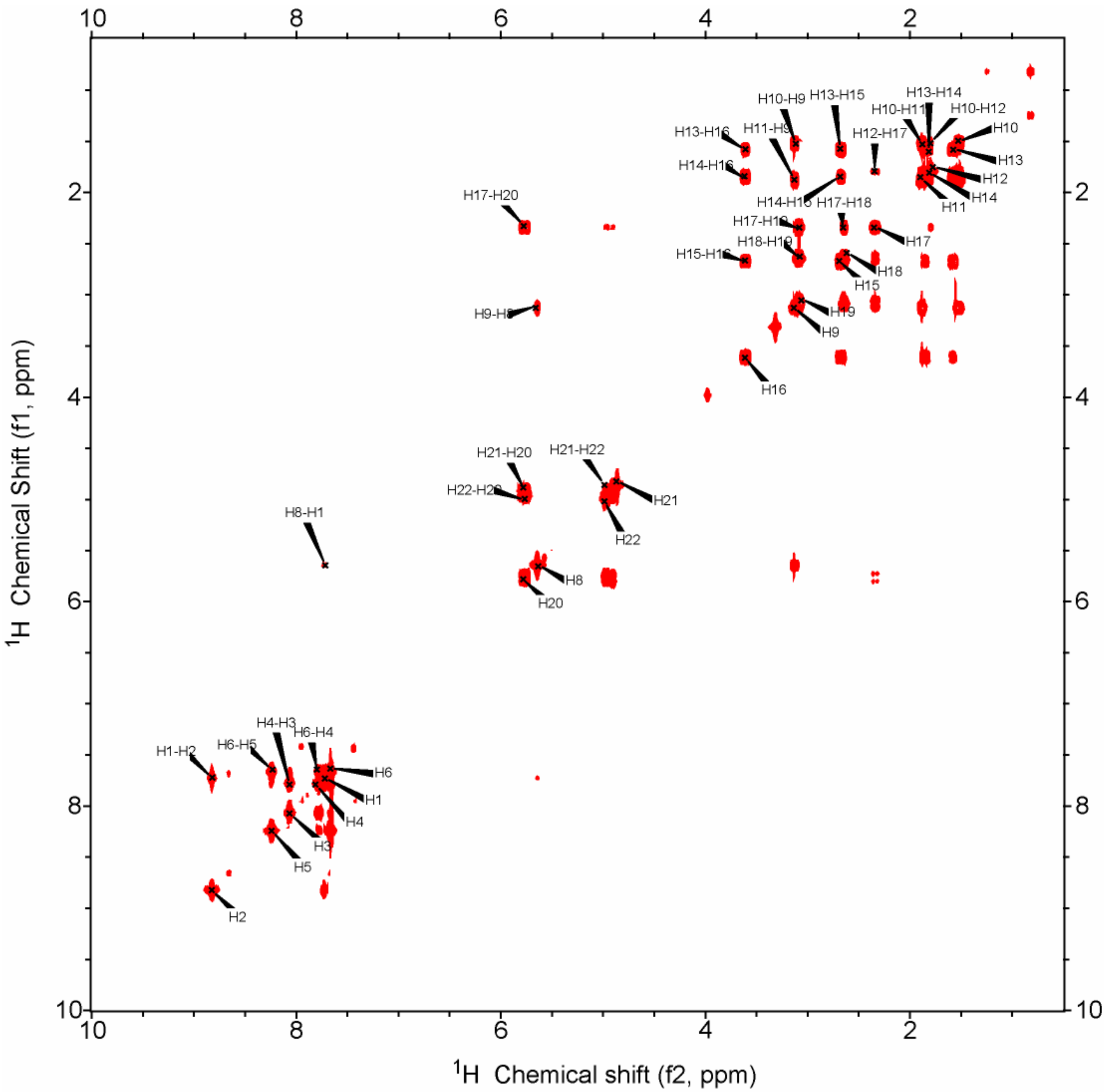
^{1}H{^{19}F} NOE Difference Experiment in CD_3CN:

1D ^{1}H{^{19}F} NOE Difference Experiment of Cinchonidine·HF in deuterated acetonitrile (bottom). Data were acquired on a 14.1 T Bruker Avance Spectrometer (^{1}H frequency 600.14 MHz) equipped with a double-resonance single-axis gradient proton-fluorine probe. 16k complex data points were acquired with a spectral width of 10.8 kHz. 16k scans were acquired with a mixing time of 900 ms and a relaxation delay of 1.5 s. For reference, the full 1D spectrum is shown above.



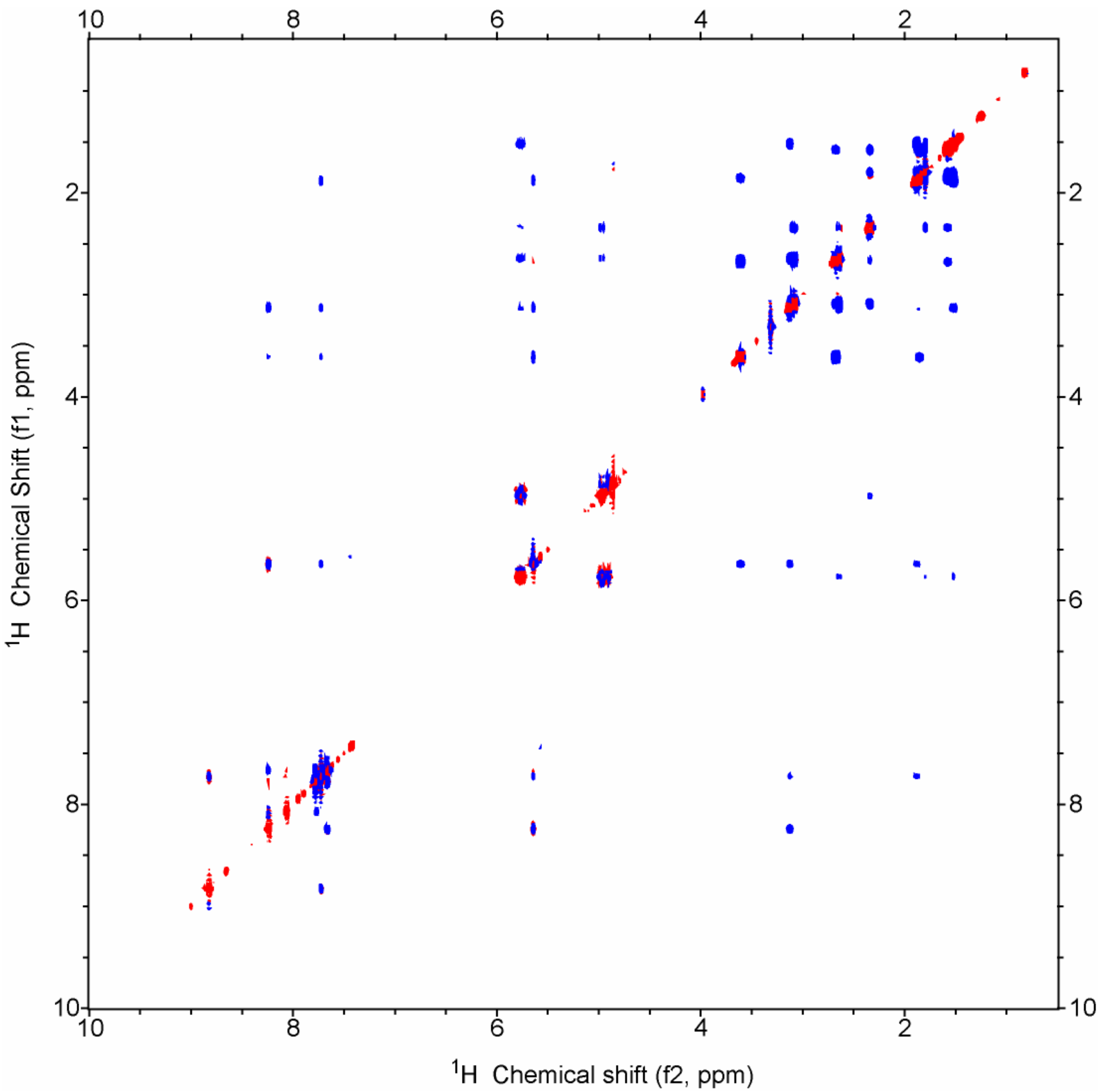
Cd: Full COSY Spectrum

2D COSY correlation spectrum of Cinchonidine in deuterated methanol. Data were acquired on a 11.7 T Varian Inova spectrometer (1H frequency 500.14 MHz) equipped with a triple-resonance triple-axis gradient probe. 256 real-valued t1 points and 2048 complex t2 points were acquired with a spectral width of 6.5 kHz in each dimension. 4 scans per t1 increment were co-added with a relaxation delay of 1 s. Spectrum was linear predicted once in the indirect dimension, and a sine-bell apodization applied to both dimensions before zero filling once and Fourier transformation.



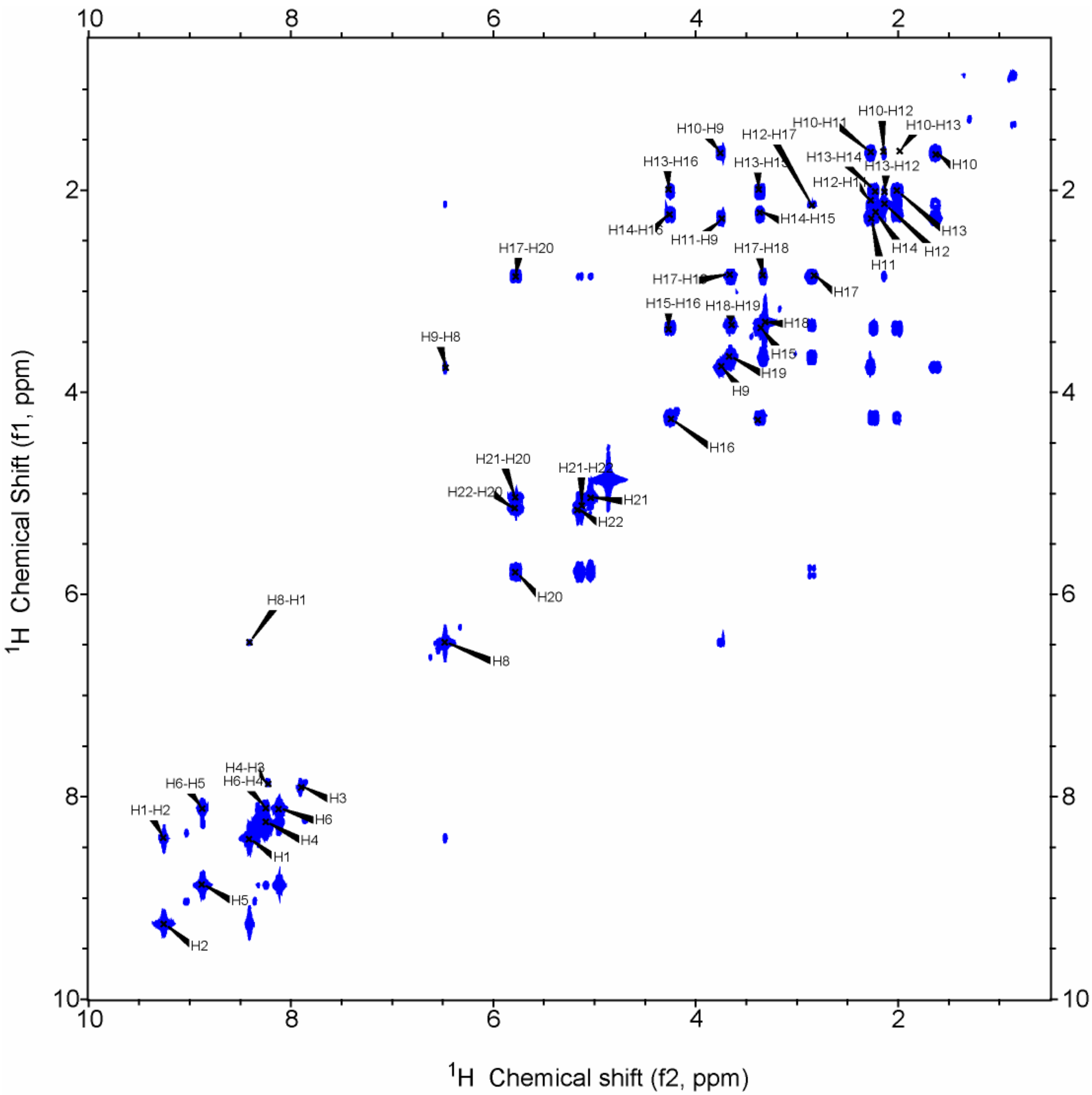
Cd: Full NOESY Spectrum

2D NOESY correlation spectrum of Cinchonidine in deuterated methanol. Data were acquired on a 11.7 T Varian Inova spectrometer (1H frequency 500.14 MHz) equipped with a triple-resonance triple-axis gradient probe. 128 complex-valued t1 points and 1024 complex t2 points were acquired with a spectral width of 6.5 kHz in each dimension. 4 scans per t1 increment were co-added with a relaxation delay of 1.5 s and a mixing time of 500 ms. Spectrum was linear predicted once in the indirect dimension, and a 90-shifted sine-bell apodization applied to both dimensions before zero filling once and Fourier transformation.



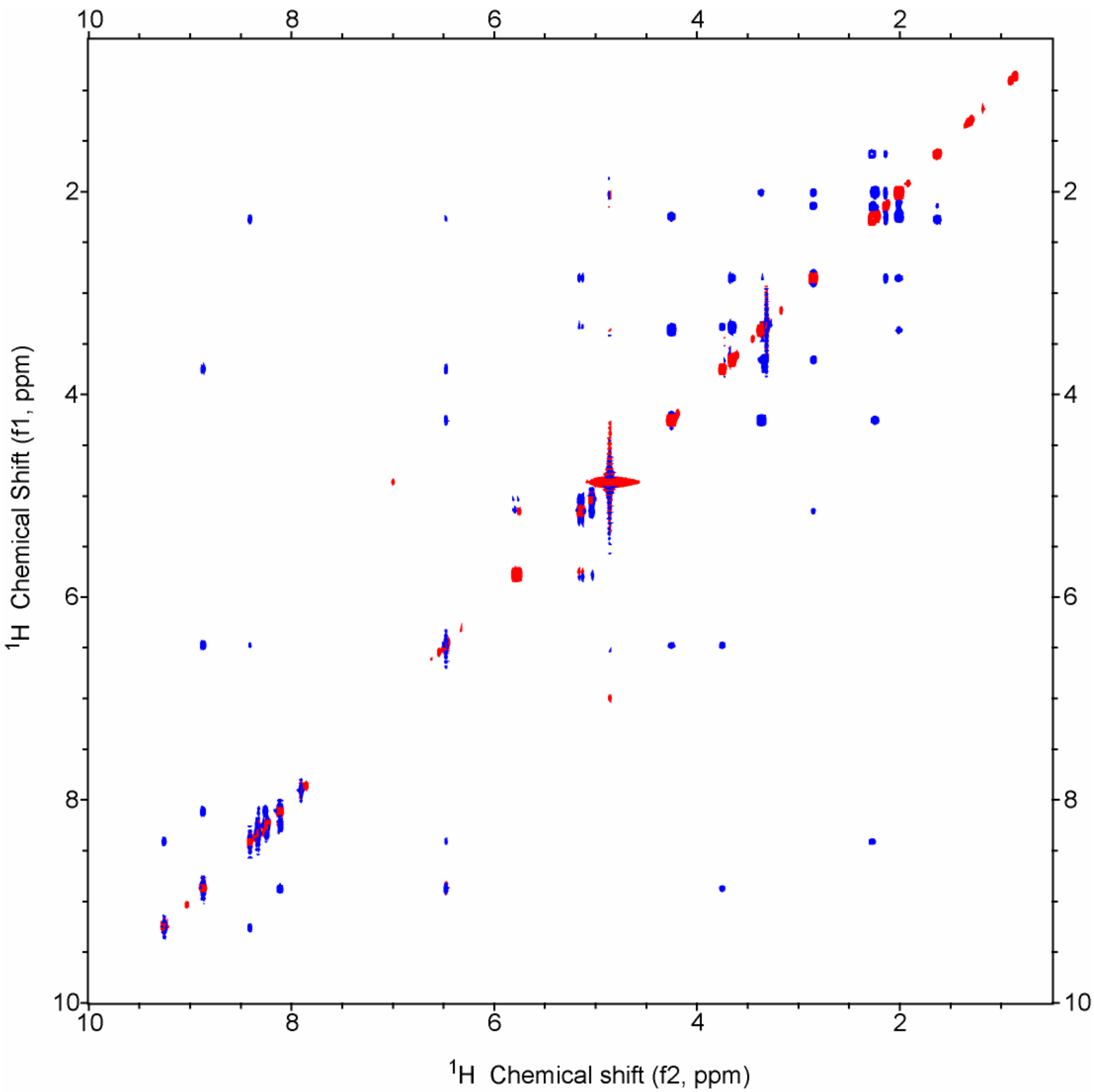
Cd·HCl: Full COSY Spectrum

2D COSY correlation spectrum of Cinchonidine in deuterated methanol. Data were acquired on a 14.1 T Bruker Avance Spectrometer (^{1}H frequency 600.14 MHz) equipped with a double-resonance single-axis gradient proton-fluorine probe. 2048 complex -valued t1 points and 4096 complex t2 points were acquired with a spectral width of 10.8 kHz in each dimension. 4 scans per t1 increment were co-added with a relaxation delay of 1 s. Spectrum was linear predicted once in the indirect dimension, and a sine-bell apodization applied to both dimensions before zero filling once and Fourier transformation.



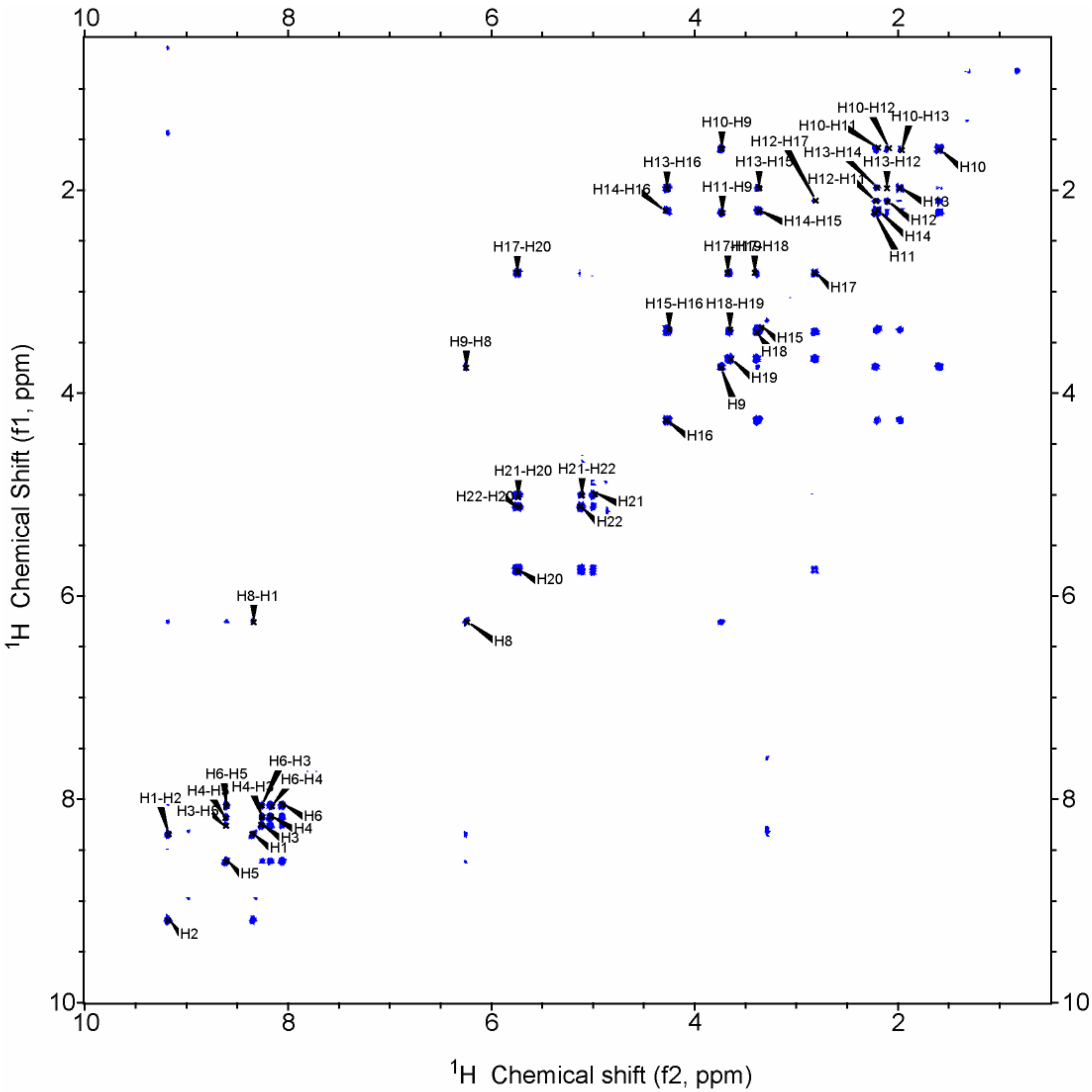
Cd·HCl: Full NOESY Spectrum

2D NOESY correlation spectrum of Cinchonidine in deuterated methanol. Data were acquired on a 14.1 T Bruker Avance Spectrometer (^{1}H frequency 600.14 MHz) equipped with a double-resonance single-axis gradient proton-fluorine probe. 1024 complex-valued t1 points and 2048 complex t2 points were acquired with a spectral width of 10.8 kHz in each dimension. 4 scans per t1 increment were co-added with a relaxation delay of 1.5 s and a mixing time of 500 ms. Spectrum was linear predicted once in the indirect dimension, and a 90-shifted sine-bell apodization applied to both dimensions before zero filling once and Fourier transformation.



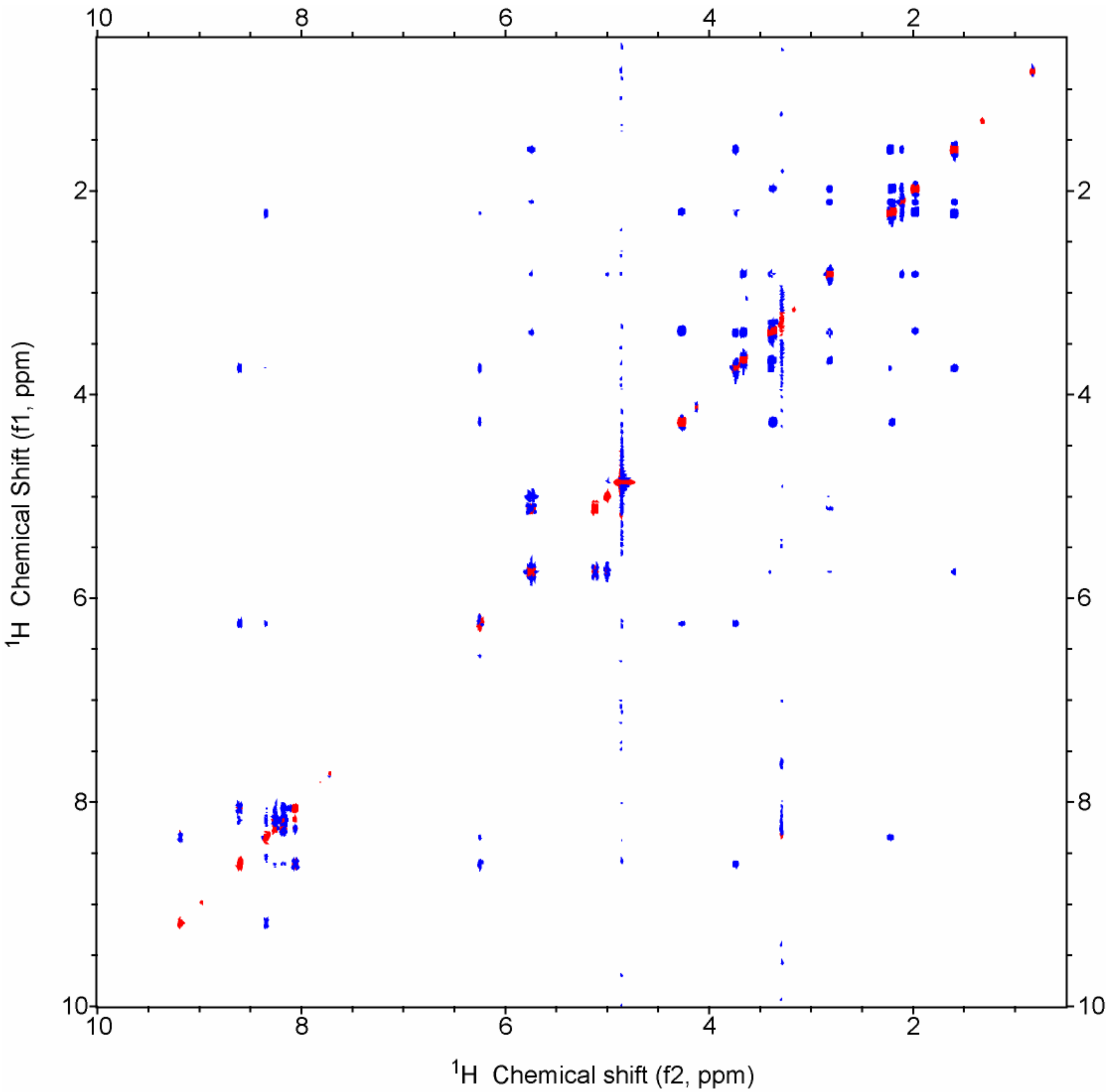
Cd·HF: Full COSY Spectrum

2D COSY correlation spectrum of Cinchonidine in deuterated methanol. Data were acquired on a 11.7 T Varian Inova spectrometer (1H frequency 500.14 MHz) equipped with a triple-resonance triple-axis gradient probe. 256 real-valued t1 points and 2048 complex t2 points were acquired with a spectral width of 6.5 kHz in each dimension. 4 scans per t1 increment were co-added with a relaxation delay of 1 s. A sine-bell apodization was applied to both dimensions before zero filling once and Fourier transformation.



Cd·HF: Full NOESY Spectrum

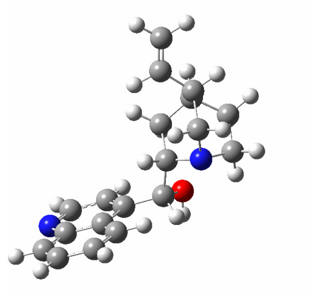
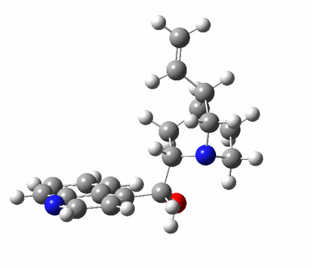
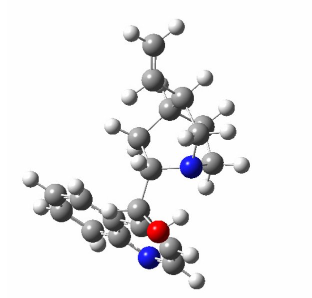
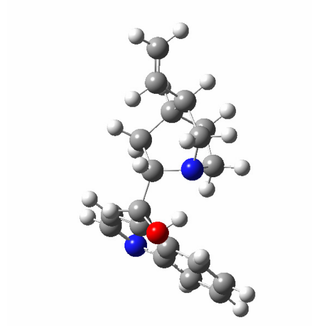
2D NOESY correlation spectrum of Cinchonidine in deuterated methanol. Data were acquired on a 11.7 T Varian Inova spectrometer (1H frequency 500.14 MHz) equipped with a triple-resonance triple-axis gradient probe. 128 complex-valued t1 points and 1024 complex t2 points were acquired with a spectral width of 6.5 kHz in each dimension. 4 scans per t1 increment were co-added with a relaxation delay of 1.5 s and a mixing time of 500 ms. A 90-shifted sine-bell apodization was applied to both dimensions before zero filling once and Fourier transformation.

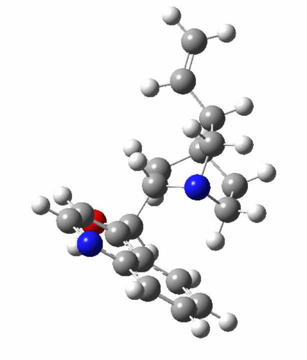
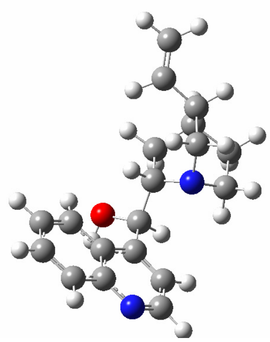


Ab Intio Structures for Lowest Energy Stable Configurations

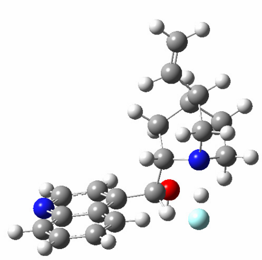
Minimum energy structures found for cinchonidine, cinchonidine·HF, and cinchonidine·HCl calculated using Gaussian03 (DFT-B3LYP; 6-31G(d,p)).

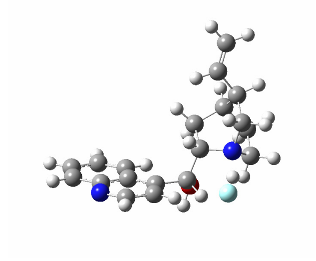
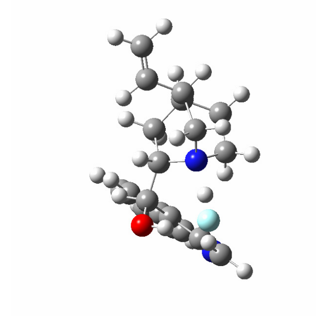
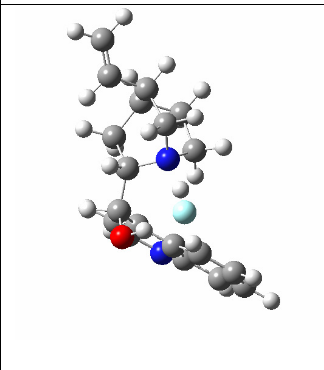
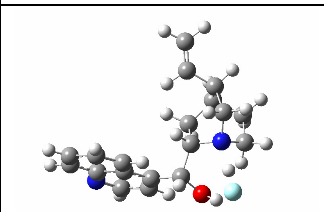
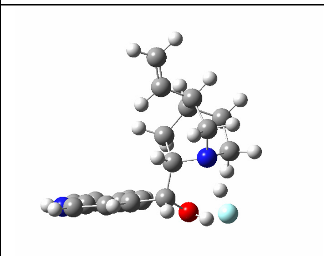
Cd Structures

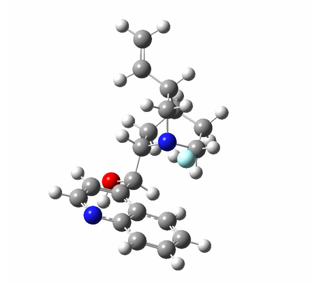
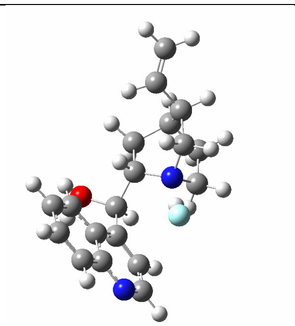
Index	Picture	C_3–C_4–C_9–C_8 torsion (degrees)	C_4–C_9–C_8–N torsion (degrees)	Rel. Energy (kcal/mol)	Rel Pop (300 K)	Description
1		102.33	152.59	0.0	0.787	Open(3)
2		-87.76	150.05	2.72	0.00821	Open(4)
3		101.45	-85.41	1.04	0.138	
4		-81.01	-88.07	2.97	0.00540	

5	NOT STABLE					Bridge(1)
6	NOT STABLE					Bridge(2)
7		84.06	68.84	2.35	0.0153	Closed(2)
8		-105.30	58.26	1.69	0.0462	Closed(1)

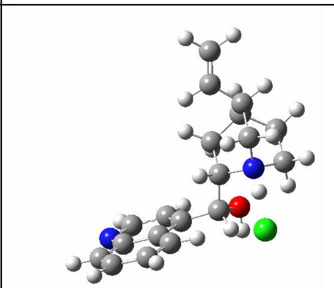
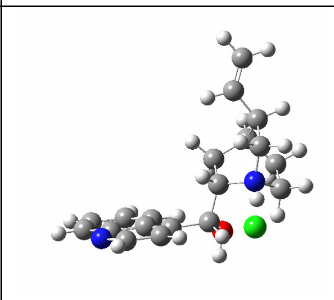
Cd·HF Structures

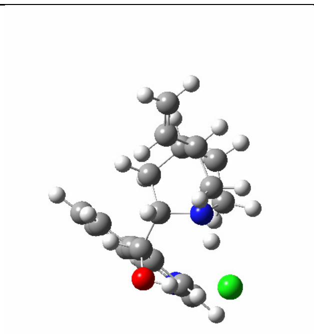
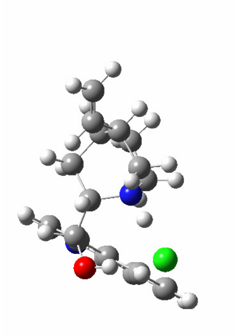
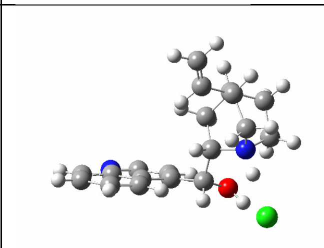
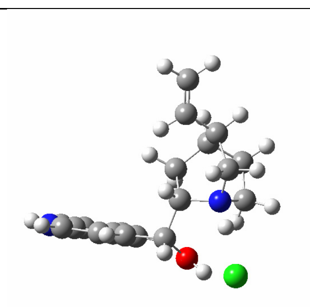
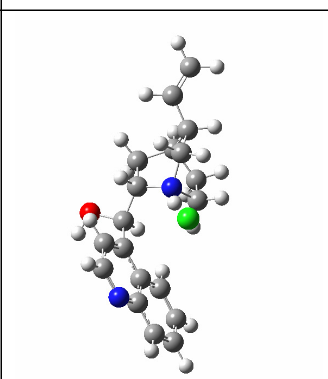
Index	Picture	C_3–C_4–C_9–C_8 torsion (degrees)	C_4–C_9–C_8–N torsion (degrees)	Rel. Energy (kcal/mol)	Rel Pop (300 K)	Description
1		101.26	154.16	0.0	0.593	Open(3)

2		-85.15	141.36	4.47	0.000328	Open(4)
3		88.82	-62.77	3.05	0.00355	
4		-90.80	-70.45	1.30	0.0669	
5		105.43	-175.75	0.36	0.324	Bridge(1)
6		-82.54	-179.38	2.29	0.0127	Bridge(2)

7		78.16	66.32	9.38	$8.69\ 10^{-8}$	Closed(2)
8		-107.94	55.45	8.82	$2.22\ 10^{-7}$	Closed(1)

Cd·HCl Structures

Index	Picture	C_3–C_4–C_9–C_8 torsion (degrees)	C_4–C_9–C_8–N torsion (degrees)	Rel. Energy (kcal/mol)	Rel Pop (300 K)	Description
1		100.06	160.11	0.76	0.212	Open(3)
2		-86.32	150.78	4.32	0.000540	Open(4)

3		93.09	-63.42	3.82	0.00125	
4		-88.57	-71.13	6.47	0.0000147	
5		107.53	-172.92	0	0.758	Bridge(1)
6		-82.43	-177.06	1.96	0.0283	Bridge(2)
7		61.44	54.98	11.95	1.49 10^{-9}	
8	NOT STABLE			X	X	

Complete Reference 17:

Abbreviated Reference:
17. Frisch, M. J., et al. *Gaussian 03*, B.05; Gaussian, Inc.: 2003.

Full Reference:

17. Gaussian 03, Revision B.05, Frisch, M. J.; Trucks, G. W.; Schlegel, H. B.; Scuseria, G. E.; Robb, M. A.; Cheeseman, J. R.; Montgomery, Jr., J. A.; Vreven, T.; Kudin, K. N.; Burant, J. C.; Millam, J. M.; Iyengar, S. S.; Tomasi, J.; Barone, V.; Mennucci, B.; Cossi, M.; Scalmani, G.; Rega, N.; Petersson, G. A.; Nakatsuji, H.; Hada, M.; Ehara, M.; Toyota, K.; Fukuda, R.; Hasegawa, J.; Ishida, M.; Nakajima, T.; Honda, Y.; Kitao, O.; Nakai, H.; Klene, M.; Li, X.; Knox, J. E.; Hratchian, H. P.; Cross, J. B.; Bakken, V.; Adamo, C.; Jaramillo, J.; Gomperts, R.; Stratmann, R. E.; Yazyev, O.; Austin, A. J.; Cammi, R.; Pomelli, C.; Ochterski, J. W.; Ayala, P. Y.; Morokuma, K.; Voth, G. A.; Salvador, P.; Dannenberg, J. J.; Zakrzewski, V. G.; Dapprich, S.; Daniels, A. D.; Strain, M. C.; Farkas, O.; Malick, D. K.; Rabuck, A. D.; Raghavachari, K.; Foresman, J. B.; Ortiz, J. V.; Cui, Q.; Baboul, A. G.; Clifford, S.; Cioslowski, J.; Stefanov, B. B.; Liu, G.; Liashenko, A.; Piskorz, P.; Komaromi, I.; Martin, R. L.; Fox, D. J.; Keith, T.; Al-Laham, M. A.; Peng, C. Y.; Nanayakkara, A.; Challacombe, M.; Gill, P. M. W.; Johnson, B.; Chen, W.; Wong, M. W.; Gonzalez, C.; and Pople, J. A.; Gaussian, Inc., Wallingford CT, 2003.