Supporting Information for

NMR Studies of Solvent-assisted Proton Transfer in a Biologically Relevant Schiff base: Distinction of Geometric and Equilibrium H-Bond Isotope Effects

Shasad Sharif, [‡] *Gleb S. Denisov,* [§] *Michael D. Toney,* [†] *and Hans-Heinrich Limbach* [‡]*

[‡] Institut für Chemie, Freie Universität Berlin, Takustraße 3, D-14195 Berlin, Germany

[§] Institute of Physics, St. Petersburg State University, 198504 St. Petersburg, Russian Federation

[†] Department of Chemistry, University of California-Davis, 95616 Davis, United States

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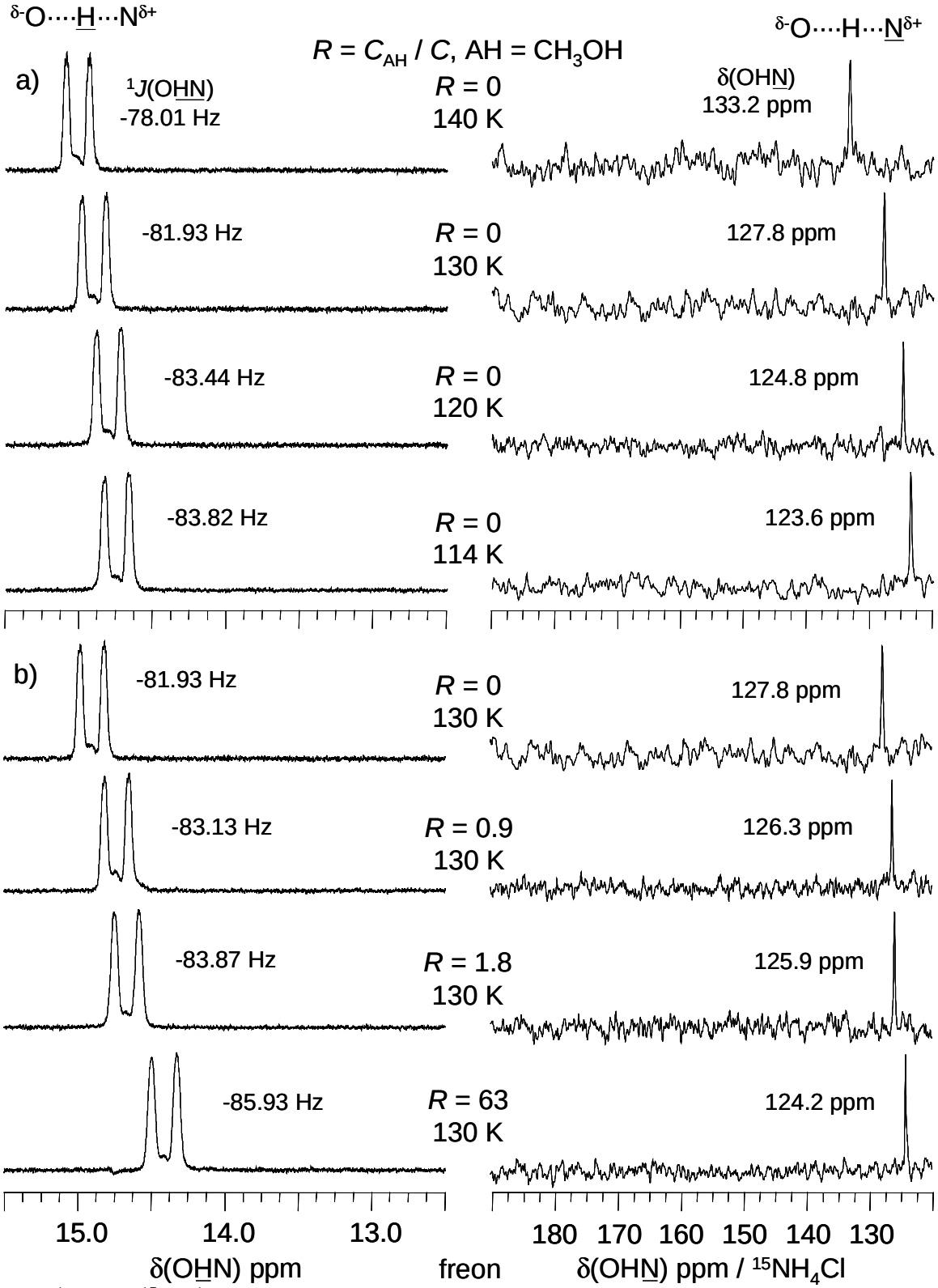


Figure S1. ^{1}H and ^{15}N {^{1}H} NMR spectra of **1** (3 mM) in deuterated freon mixture CDF_3 / $CDClF_2$, with a CHF_3 molar fraction of N = 0.41. a) Variation of the temperature from 140 to 114 K. b) add defined ratios $R = C_{AH} / C$ of alcohol, with AH = CH_3OH methanol. The ratios of methanol R were estimated by integration of ^{1}H signals.

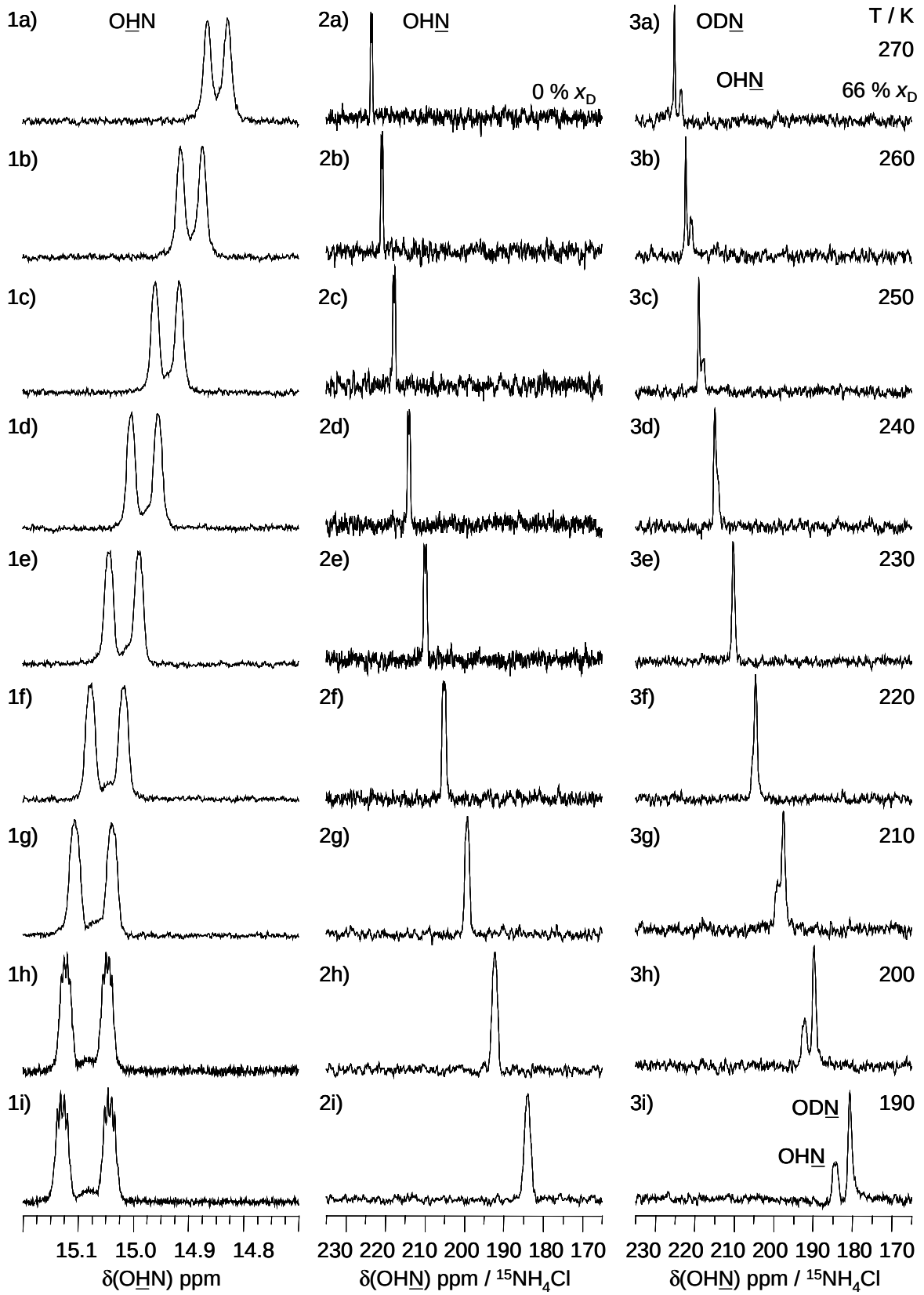


Figure S2. Spectra of **1** in CD_2Cl_2 in a temperature range of 270 to 190 K. 1 a-i) ^{1}H NMR of **1** (2 mM). 2 a-i) ^{15}N NMR of none ^{1}H decoupled of **1** (30 mM). 3 a-i) ^{15}N NMR of none ^{1}H decoupled of deuterated **1** (45 mM). The deuteration ratio x_D of 66 % was estimated by integration of ^{1}H signals.

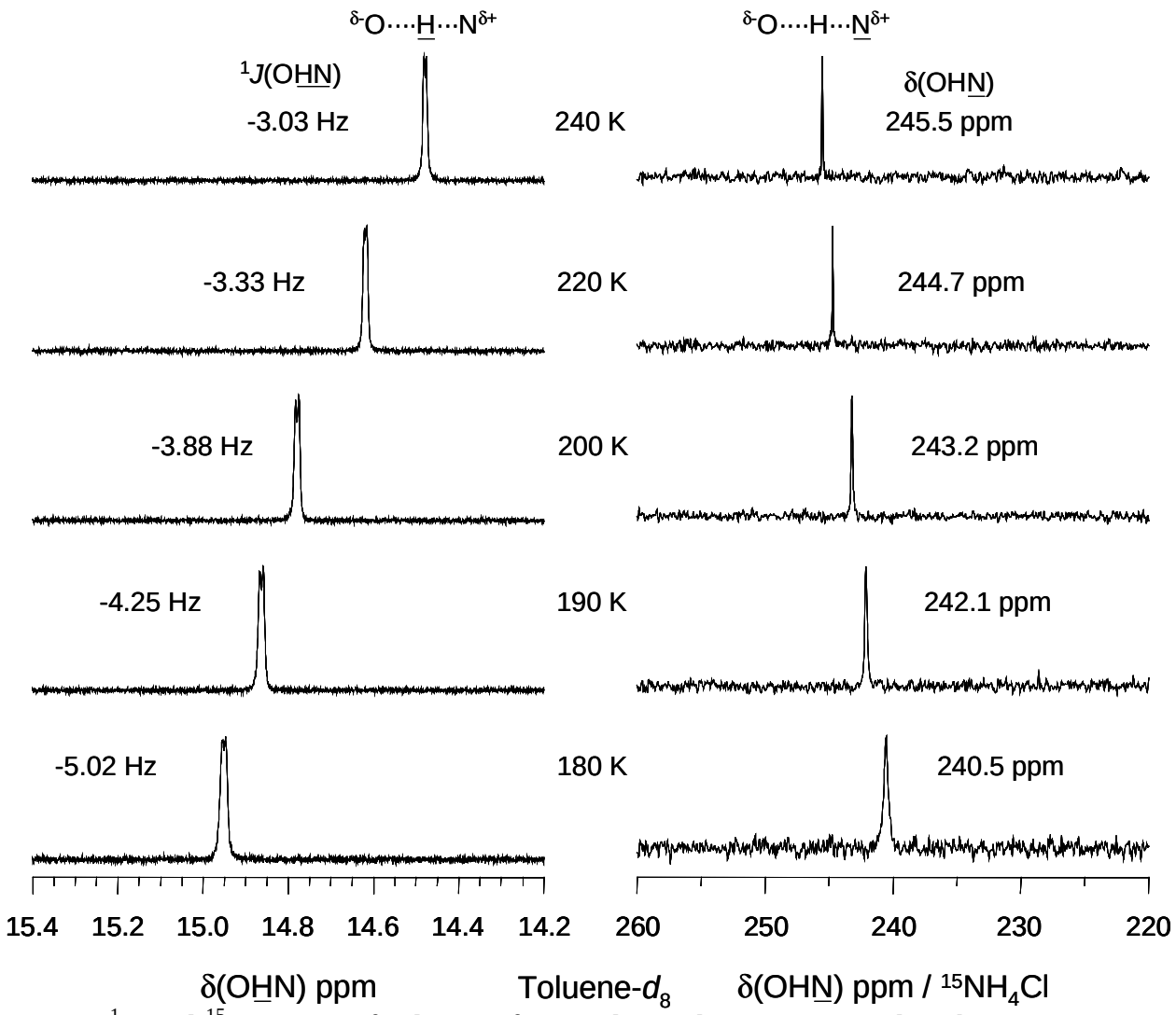


Figure S3. ^{1}H and ^{15}N spectra of solution of **1** in toluene-d_8 were measured in the temperature range 180-240 K; concentrations of **1** were 2 mM for ^{1}H NMR and 15 mM for ^{15}N NMR spectra.

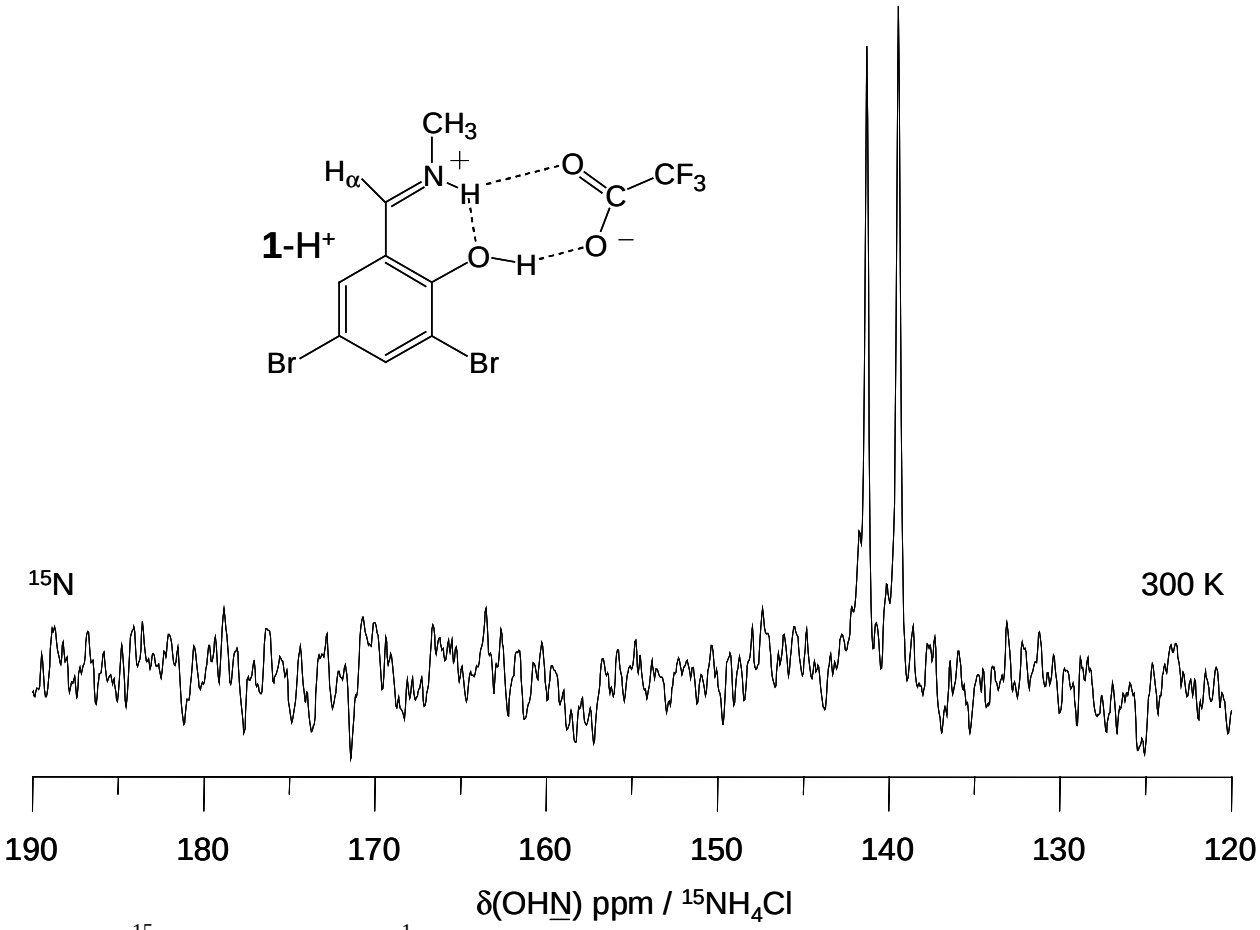


Figure S4. ^{15}N NMR of none ^{1}H decoupled spectra of **1** in trifuoroacetic acid at 300 K, with δ(OH<u>N</u>) = 149.68 ppm and ^{1}J(O<u>HN</u>) = -93.86 Hz. The spectrum was recorded by locking on a capillary with trifluoroacetic acid-d_1.

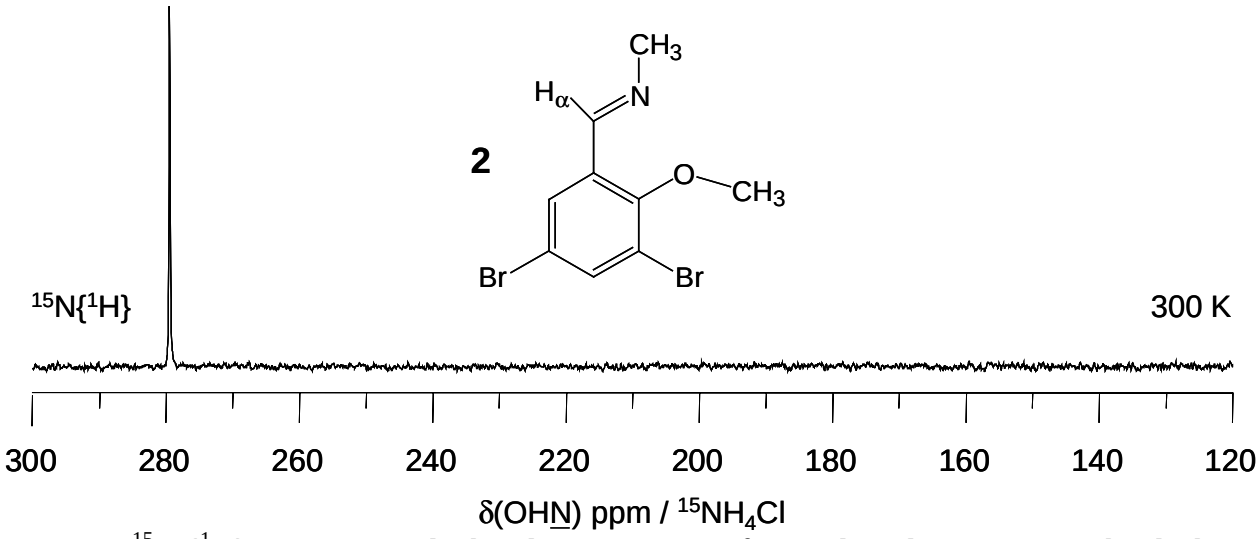


Figure S5. ^{15}N {^{1}H} NMR natural abundance spectra of neat liquid **2** at 300 K by locking on dichloromethane-d_2 capillary, with δ(OH<u>N</u>) = 279.5 ppm.

Table S1. Temperature dependent of the static dielectric constant ε_r of non- and protic organic solvents: $CHCl_3$, CH_2Cl_2, CH_3OH and $CH_3C_6H_5$ (toluene).

experimental values of the static dielectric constant ε_r								**calculated static dielectric constant ε_r**					
$CHCl_3$		**CH_2Cl_2**		**CH_3OH**		**Tol.**			**Freon**	**$CHCl_3$**	**CH_2Cl_2**	**CH_3OH**	**Tol.**
T / K	**ε_r**	**T / K**	**ε_r**	**T / K**	**ε_r**	**T / K**	**ε_r**	**T / K**	**ε_r [a)]**	**ε_r**	**ε_r**	**ε_r**	**ε_r**
333.15	4.12	313.15	8.29	333.15	26.55	383.15	2.140	350	3.41	3.95	7.34	25.55	2.24
323.15	4.29	303.15	8.71	323.15	27.45	363.15	2.180	340	3.84	4.08	7.63	26.60	2.26
313.15	4.47	293.15	9.14	313.15	29.01	348.15	2.218	330	4.30	4.22	7.93	27.71	2.27
303.15	4.65	283.15	9.58	303.15	30.80	323.15	2.287	320	4.79	4.36	8.25	28.90	2.29
293.15	4.84	273.15	10.02	298.15	31.50	298.15	2.373	310	5.32	4.52	8.59	30.16	2.31
283.15	5.02	263.15	10.51	293.15	32.35	288.15	2.373	300	5.88	4.69	8.96	31.50	2.32
273.15	5.22	253.15	11.00	283.15	34.05	278.15	2.397	290	6.48	4.87	9.35	32.94	2.34
263.15	5.43	243.15	11.56	273.15	35.80	273.15	2.408	280	7.12	5.06	9.77	34.47	2.37
253.15	5.65	233.15	12.14	263.15	37.50	253.15	2.462	270	7.82	5.26	10.22	36.13	2.39
243.15	5.89	223.15	12.77	233.15	44.00	233.15	2.519	260	8.57	5.48	10.70	37.91	2.41
233.15	6.16	213.15	13.49	203.15	51.50	213.15	2.569	250	9.39	5.72	11.23	39.83	2.44
223.15	6.45	203.15	14.23	173.15	60.00	193.15	2.617	240	10.28	5.98	11.79	41.91	2.47
213.15	6.79	193.15	15.05			177.65	2.669	230	11.26	6.26	12.41	44.17	2.50
		183.15	15.97			383.15	2.140	220	12.32	6.57	13.08	46.64	2.53
		173.15	16.98			363.15	2.180	210	13.50	6.91	13.82	49.34	2.57
								200	14.80		14.63	52.32	2.61
								190	16.26		15.52	55.60	2.66
								180	17.88		16.52	59.26	2.71
								170	19.72		17.63	63.34	2.76
								160	21.81				
								150	24.20				
								140	26.98				
								130	30.24				
								120	34.12				
								110	38.81				
								114	36.82				

[a] Freon mixture with a mole fraction of N = 0.41 using an empirical relation. References of the experimental values of ε_r are mention in the article.

<u>Complete Ref. 37:</u>

M. J. Frisch, G.W. Trucks, H. B. Schlegel, G. E. Scuseria, M. A. Robb, J. R. Cheeseman, V. G. Zakrzeswski, J. A. Montgomery, Jr., R. E. Stratman, J. C. Burant, S. Dapprich, J. M. Millam, A. D. Daniels, K. N. Kudin, M. C. Strain, O. Farkas, J. Tomasi, V. Barone, M. Cossi, R. Cammi, B. Mennucci, C. Pomelli, C. Adamo, S. Clifford, J. Ochterski, G. A. Petersson, P. Y. Ayala, Q. Cui, K. Morokuma, D. K. Malick, A. D. Rabuck, K. Raghavachari, J. B. Foresman, J. Cioslowski, J. V. Ortiz, A. G. Baboul, B. B. Stefanov, G. Liu, A. Liashenko, P. Piskorz, I. Komaromi, R. Gomperts, R. L. Marin, D. J. Fox, T. Keith, M. A. Al-Laham, C. Y. Peng, A. Nanayakkara, C. Gonzalez, M. Challacombe, P.M.W. Gill, B. Johnson, W. Chen, M. W. Wong, J. L. Andres, C. Gonzales, M. Head-Gordon, E. S. Replogle, and J. A. Pople, *Gaussian98*, 98 ed., Gaussian, Inc., Pittsburgh, PA (1998).

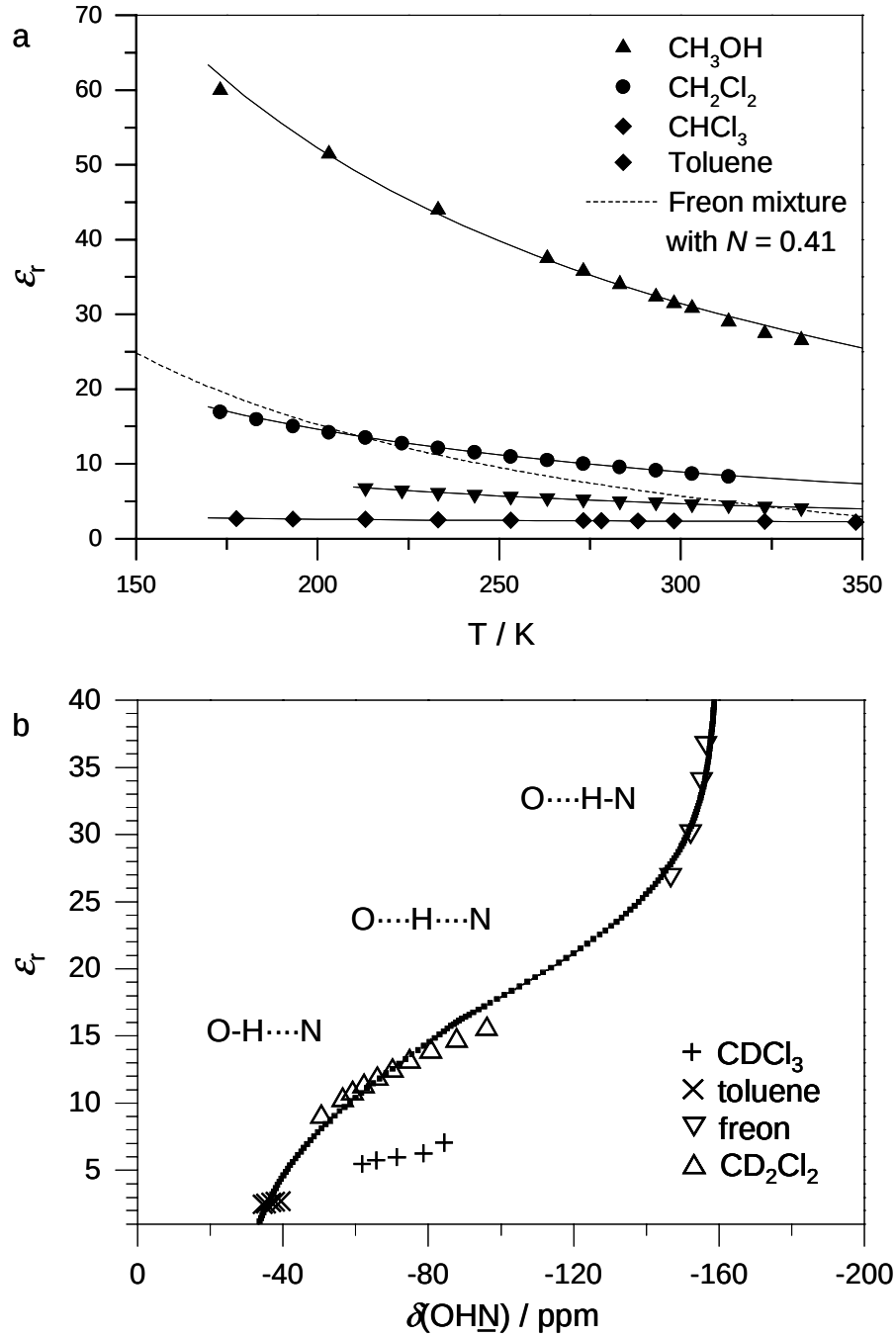
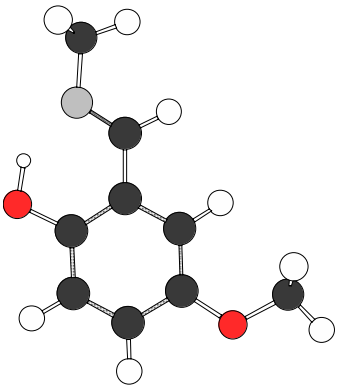
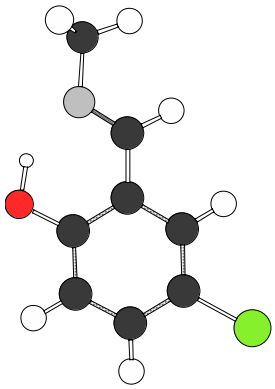


Figure S6. a) Temperature dependent of the static dielectric constant ε_r in different aprotic organic solvents, experimental values are listed in Table S2. b) The static dielectric constant ε_r *vs.* δ(OH<u>N</u>) chemical shifts, using different parameters for the ^{15}N chemical shift δ(<u>N</u>)° = -25 ppm and δ(H<u>N</u>)° = -160 ppm. The empirical relation $\varepsilon_r(q_1^H) = 28\ q_1^H + 17$ was used.

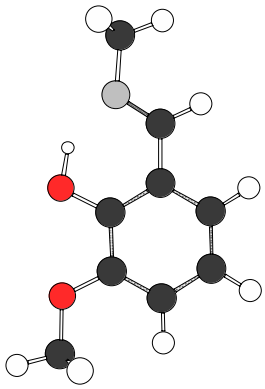
Scheme S1. Overview of with density function method calculated structures in the dominant tautomeric form, optimized with B3LYP/6-31++G*, of N-(R_1-salicylidene)-alkyl(R_2)amines.



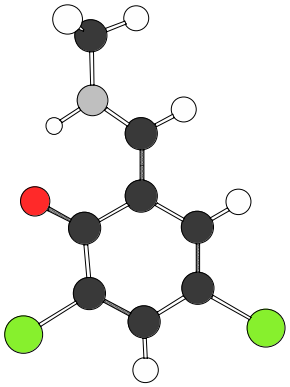
A N-(5-methoxysalicylidene)-methylamine



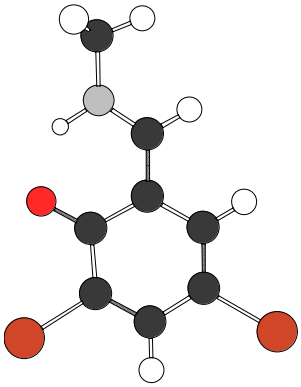
B N-(5-chlorosalicylidene)-methylamine



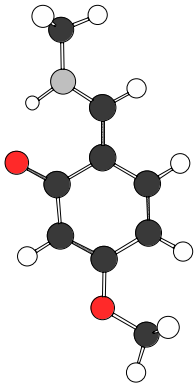
C N-(3-methoxysalicylidene)-methylamine



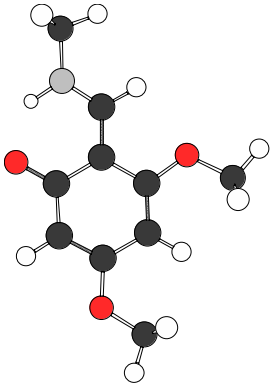
D N-(3,5-dichlorosalicylidene)-methylamine



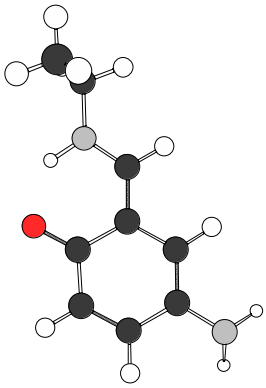
E N-(3,5-dibromosalicylidene)-methylamine



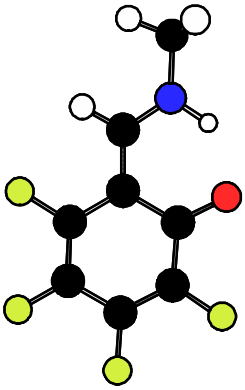
F N-(4-methoxysalicylidene)-methylamine



G N-(4,6-dimethoxysalicylidene)-methylamine



H N-(5-nitrosalicylidene)-ethylamine



I N-(3,4,5,6-tetrafluorosalicylidene)-methylamine

Table S2. Calculated geometries and energies of the intramolecular OHN hydrogen bond and over GIAO calculated ^{15}N chemical shifts of the tautomer *a* (OH-form) and *b* (NH-form) of N-(R_1-salicylidene)-alkyl(R_2)amines.

	tautomer *b* (NH-form)												
	N-(R_1-salicylidene)-alkyl(R_2)amines	**R_1**	**R_2**	**δ(N) / ppm**	**E / a. u.**	**ZPE / a. u.**	**r_{NO} / Å**	**r_{OH} / Å**	**r_{NH} / Å**	**α(OHN) / °**	**r_{NO} / Å**	**GIAO / ppm**	**GIAO[b] / ppm**
A	N-(5-methoxy-	5-OCH_3	-CH_3	254.9[a]	-554.777845667	0.187735	2.603666	1.740777	1.038465	137.6118		121.5208	79.065
B	N-(5-chloro-	5-Cl	-CH_3	240.9[a]	-899.849347615	0.145663	2.603017	1.734042	1.040575	138.0983	2.559[c]	113.0178	87.568
C	N-(3-methoxy-	3-OCH_3	-CH_3	243.6[a]	-554.775928572	0.188007	2.601626	1.741352	1.038196	137.3245		117.4351	83.151
D	N-(3,5-dichloro-	3,5-diCl	-CH_3	126.8[a]	-1359.442283060	0.136209	2.602221	1.741303	1.038634	137.3551	2.574[c]	109.6718	90.914
E	N-(3,5-dibromo-	3,5-diBr	-CH_3	127.6[a]	-5582.513276060	0.137960	2.596136	1.731140	1.039796	137.6806		108.7797	91.807
F	N-(4-methoxy-	4-OCH_3	-CH_3	106.9[a]	-554.782098937	0.187556	2.598732	1.722067	1.042823	138.7521		116.9000	83.686
G	N-(4,6-dimethoxy-	4,6-diOCH_3	-CH_3	101.8[a]	-669.310555994	0.220496	2.592138	1.722231	1.040858	138.129		119.8312	80.755
H	N-(5-nitro-	5-NO_2	-C_2H_5	140.3[a]	-534.924523923	0.200274	2.606804	1.742634	1.039034	137.7148	2.646[c]	103.1786	97.408
I	N-(3,4,5,6-tetrafluoro-	3,4,5,6-F	-CH_3	--	-837.193198776	0.122870	2.618343	1.763738	1.036414	136.9316		109.4719	91.114
	tautomer *b* (OH-form)												
	N-(R_1-salicylidene)-alkyl(R_2)amines	**R_1**	**R_2**	**δ(N) / ppm**	**E / a. u.**	**ZPE / a. u.**	**r_{NO} / Å**	**r_{OH} / Å**	**r_{NH} / Å**	**α(OHN) / °**		**GIAO / ppm**	**GIAO[b] / ppm**
A	N-(5-methoxy-	5-OCH_3	-CH_3	254.9[a]	-554.782490376	0.187696	2.659814	0.996523	1.773245	146.2095		-63.5322	264.118
B	N-(5-chloro-	5-Cl	-CH_3	240.9[a]	-899.853690810	0.145623	2.653177	0.998526	1.763133	146.426	2.559[c]	-68.3221	268.908
C	N-(3-methoxy-	3-OCH_3	-CH_3	243.6[a]	-554.779623701	0.187912	2.651550	0.997898	1.759075	146.8863		-63.7325	264.319
D	N-(3,5-dichloro-	3,5-diCl	-CH_3	126.8[a]	-1359.444593060	0.135919	2.635884	1.001511	1.738696	147.0302	2.574[c]	-70.1466	270.733
E	N-(3,5-dibromo-	3,5-diBr	-CH_3	127.6[a]	-5582.515873110	0.137816	2.634931	1.001362	1.737837	147.0345		-69.0622	269.648
F	N-(4-methoxy-	4-OCH_3	-CH_3	106.9[a]	-554.787103947	0.187686	2.655916	0.998826	1.761467	147.0704		-53.5026	254.089
G	N-(4,6-dimethoxy-	4,6-diOCH_3	-CH_3	101.8[a]	-669.312668290	0.220406	2.619465	1.003993	1.714221	147.873		-45.5216	246.108
H	N-(5-nitro-	5-NO_2	-C_2H_5	140.3[a]	-534.930091417	0.200226	2.667304	0.995361	1.781703	146.2552	2.646[c]	-81.722	282.308
I	N-(3,4,5,6-tetrafluoro-	3,4,5,6-F	-CH_3	--	-837.192597992	0.122306	2.626541	1.004557	1.726921	146.9241		-69.7598	270.346

Method: DFT (B3LYP/6-311++G(d,p)//B3LYP/6-31++G(d)). ^{15}N chemical shift are referenced to external solid $^{15}NH_4Cl$. [a] ^{15}N chemical shifts in solid state of **A** to **H** reported from Kamienski *et al.*, A. *Solid State NMR* 2000, *16*, 285-289. [b] σ from GIAO calculated ^{15}N chemical shifts, conversion $\delta = 257.868 - \sigma$ by recalculation it to solid $^{15}NH_4Cl$ with -57.282 ppm. [c] crystallographic distances are obtained for **B** and **D** from Filarowski *et al.*, *Berichte der Bunsen-Gesellschaft* 1998, *102*, 393-402 and for **H** from Krygowski*et al.*, *Journal of Physical Chemistry A* 1997, *101*, 9399-9404.