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Conformational Equilibria of Ethanolamine and Its Hydrochloride in Solution

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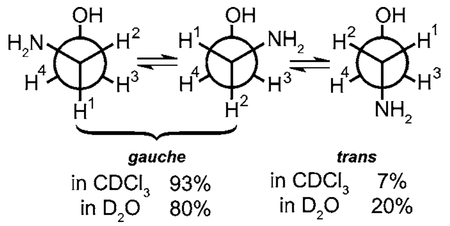
ABSTRACT



The conformational preferences of ethanolamine and its hydrochloride in solution were estimated by comparing experimental NMR vicinal proton–proton coupling constants to semiemprical coupling constants for each staggered rotamer, derived by the Haasnoot–Altona method. Strong *gauche* preferences are observed for both ethanolamine and its hydrochloride over a wide range of solvent polarities. Concentration was not observed to significantly affect the position of the conformer equilibria.

Ethanolamine (2-aminoethanol; MEA) is used in aqueous solution in industrial processes, including CO_2 sequestration.[1] Structurally, MEA is related to 1,2-substituted ethanes whose conformational equilibria have been studied in our research, including ethylene glycol[2] and ephedrine.[3] Although microwave[4,5] and ab initio[6] studies conducted on MEA in the gas phase concurred in finding a strong *gauche* preference with an intramolecular OH−N bond, preferences for MEA in solution have been a subject of some disagreement. Infrared[7,8] and dipole moment[9] studies have reported a *gauche* preference for MEA in nonpolar solutions, while another infrared study[10] taking account of NMR chemical shift data reported a *trans* preference. A Raman spectroscopy study qualitatively detected both *trans* and *gauche* conformers in aqueous solution and suggested that the *gauche* form was likely to be more prevalent.[11] Molecular dynamics studies of MEA in aqueous solution have variously reported *gauche* preferences[12,13] or, depending on the way the conformational equilibria were calculated, quite variable values with concentration but nonetheless leading to an overall conclusion of essentially exclusive preferences for *gauche* in concentrated solutions (mole fraction 0.8−1.0), decreasing to yield a significant *trans* preference at lower concentration (mole fraction 0.03−0.1).[14]

In this research, the conformational preferences of MEA and its hydrochloride were estimated in several deuterated solvents by fitting semiemprical constants for each rotamer derived by the Haasnoot−Altona method[15] to observed, time-

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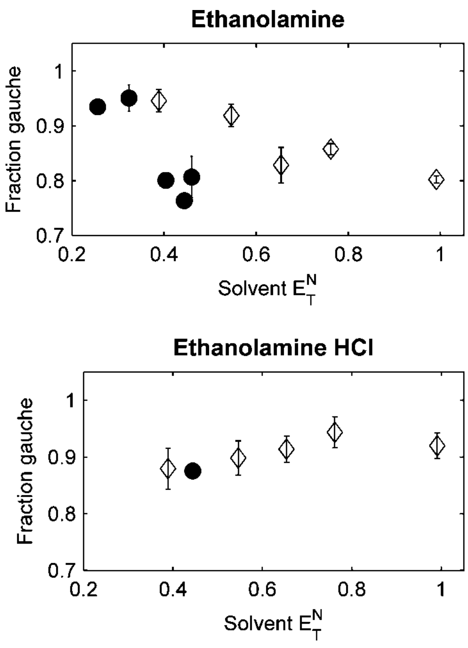

Figure 1. Fractions of *gauche* plotted against solvent E_T^N. Protic solvents are indicated by diamonds and aprotic solvents by filled circles. Solvents are identified in Table 1.

averaged vicinal proton−proton coupling constants. The NMR spectra were taken at 300 MHz at the ambient temperature. Sample concentrations were ∼0.5 M unless otherwise specified, and peaks were referenced to TMS or to DSS in D_2O. Coupling constants were extracted from the spectra by iterative simulations with gNMR.[16] Compounds were at least 99% pure and were used without further purification. Ethanolamine hydrochloride was synthesized from the free base by the method previously reported by Yang et al.[17]

Ethanolamine is seen to exhibit a strong *gauche* preference in all solvents examined. In Figure 1, the percentages of *gauche* for MEA and MEA•HCl in each solvent are plotted against the empirical Dimroth and Reichardt[18] solvent polarity parameter E_T^N.[19] To calculate the percentage of *gauche*, we started by taking *gauche* dihedral angles to be 60° and *trans* angles to be 180°, which are supported by simulation results.[13] For each spectrum, two independent estimates of the conformer populations can be obtained by simple algebra from the experimental couplings $^3J_{13}$ and $^3J_{14}$ (where $^3J_{23} = {}^3J_{14}$ and $^3J_{24} = {}^3J_{13}$), with predicted values of $^3J_{13}$ and $^3J_{14}$ for each of the MEA and MEA•HCl conformers obtained from the Haasnoot−Altona procedures.[15] However, the two estimated populations derived for any given sample tended to differ by a rather unsatisfactory 10% or more for ethanolamine. Nonetheless, the differences between the estimates from $^3J_{13}$ and $^3J_{14}$ seemed to behave in a systematic manner, which suggests that either inappropriate dihedral angles or λ values[15] were used in the Altona equation.[15c] Agreement between these estimates turned out to be quite sensitive to the values of the dihedral angles. For ethanolamine, we minimized disagreement across the data set by using *gauche*/*trans* angles of 55.9°/175.9°, which yielded significantly better results than the perfectly staggered 60°/180° pair. Our choice of angle is generally consistent with gas-phase microwave[4] (55.4 ± 2°) and aqueous solution simulation[12] (59.8°) results. In D_2O, which was parametrized separately in the Haasnoot−Altona method, we found minimum disagreement at 57.9°/177.9°. For the hydrochloride, 60°/180° angles were found to give good results. Figure 1 is a plot of the average of the conformer population estimates with "error bars" representing the separate values derived from $^3J_{13}$ and $^3J_{14}$. Table 1 shows the experimental

Table 1. Predicted and Experimental ^3J Values with Estimated Percentage *gauche* from Each, with Solvents Ordered by Ascending E_T^N

		ethanolamine					ethanolamine HCl				
solvent (deuterated)	$E_T^{N\,a}$	$^3J_{13}$	% *g* ($^3J_{13}$)	$^3J_{14}$	% *g* ($^3J_{14}$)	mean % *g*	$^3J_{13}$	% *g* ($^3J_{13}$)	$^3J_{14}$	% *g* ($^3J_{14}$)	mean % *g*
100% *gauche*[b]		*6.53*		*3.44*			*6.86*		*2.97*		
100% *gauche* (D_2O)[b]		*6.78*		*3.25*			*7.14*		*3.09*		
100% *trans*[b]		*5.41*		*11.92*			*4.50*		*12.28*		
100% *trans* (D_2O)[b]		*4.93*		*12.13*			*4.40*		*12.50*		
					Aprotic						
chloroform	0.256	6.46	*94*	4.03	*93*	**93**					
nitrobenzene	0.324	6.50	*97*	4.06	*93*	**95**					
dimethylformamide	0.404	6.30	*80*	5.09	*81*	**80**					
DMSO	0.444	6.25	*75*	5.34	*78*	**76**	6.59	*89*	4.23	*86*	**88**
acetonitrile	0.460	6.27	*77*	4.76	*84*	**81**					
					Protic						
tert-butyl alcohol	0.389	6.49	*97*	4.07	*93*	**95**	6.66	*93*	4.43	*84*	**88**
isopropyl alcohol	0.546	6.46	*94*	4.30	*90*	**92**	6.69	*93*	4.20	*87*	**90**
ethanol	0.654	6.30	*80*	4.62	*86*	**83**	6.71	*94*	3.99	*89*	**91**
methanol	0.762	6.38	*87*	4.73	*85*	**86**	6.79	*97*	3.75	*92*	**94**
D_2O	0.991	6.41	*80*	4.86	*81*	**80**	6.89	*91*	3.74	*93*	**92**

[a] From ref 18. [b] Estimated values predicted by the Haasnoot−Altona methods (ref 15).

coupling constants and the percentage of *gauche* calculated for each, along with the Altona coupling constants predicted for MEA and MEA·HCl.[15c] The λ values for $-NH_2$, $-NH_3^+$, and $-OH$ were as listed by Altona and co-workers.[15c]

In light of molecular dynamics simulation results[14] suggesting that ethanolamine may have dramatically concentration-dependent conformational behavior in aqueous solution, 0.03, 0.1, and 0.3 mole fraction solutions of ethanolamine were prepared in D_2O without DSS, matching the lower, *trans*-favoring concentrations reported in the molecular dynamics study.[14] Only small changes in the conformational equilibria were observed (Figure 2). The most notable solvent effect on the conformations of ethanolamine is the reduced percentage *gauche* observed in DMSO, acetonitrile, and DMF, all of which are aprotic and good hydrogen-bond acceptors. In other solvents, the *gauche* preference of ethanolamine roughly decreases with increasing solvent polarity, from 93% in chloroform to 80% in D_2O. Ethanolamine's behavior is perhaps surprising in light of ethylene glycol's tendency to prefer its *gauche* conformation more strongly in more polar solutions.[2] Furthermore, many of the factors thought to stabilize *gauche* conformers, including the gauche effect and solvent−solute dipole interactions, should be stronger in polar solutions. Some insight may be gained from the fact that the solvent-dependent conformational behavior of ethanolamine is more linear when plotted against the solvent's E_T^N than against its dielectric constant.[19] The E_T^N scale is known to reflect both solvent polarity and hydrogen-bonding acidity,[18] which suggests that solvent−solute hydrogen bonding may play an important role in creating this difference. It seems very reasonable that steric influences arising from solvation by protic solvents to the MEA's amine or hydroxyl groups should perturb, to at least some degree, the conformational preferences away from the *gauche* conformers. However, to our continuing surprise, we have not yet found credible examples of such influences in any of our prior studies of conformational preferences.

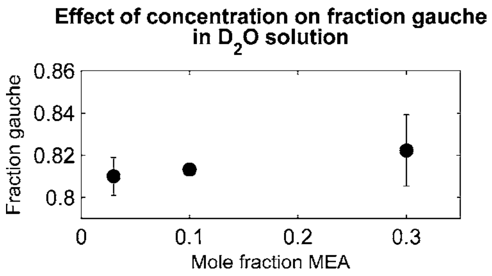

Figure 2. MEA preference for *gauche*, plotted against concentration in D_2O solution.

The conformational equilibria of MEA·HCl display a weak opposite trend with solvent polarity relative to MEA, from 88% *gauche* in DMSO to 94% in methanol but declining to 92% in D_2O. The *gauche* effect, hydrogen bonding, steric influences, and the simple polar solvent effect can each arguably be expected to increase the preference for *gauche* with increasing solvent polarity, but because the effect is quite small, it seems best to see if a more definitive case could be found to sort out which of the cited effects (or others) are the more important.

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