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Theoretical study of solvent effect on NMR shielding for Pyrazole and Pyrazoline

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ABSTRACT

The physical and chemical properties of Pyrazole and Pyrazoline molecules were theoretically studied by Gaussian 03, software with NMR and Molecular orbital calculations at B3LYP/6-31G and B3LYP/6-31+G(d) levels, in gas phase and solution. In this study a comparison effect of three solvents with different dielectric constants on Pyrazole and Pyrazoline molecules in aspect energy interaction between solute and solvent, and NMR shielding parameters (ppm) such as, σ_{Iso} (σ Isotropic), σ_{Aniso} (σ Anisotropic), anisotropic magnetic shielding tensor, $\Delta\sigma$, chemical shift, δ, total atomic charge and asymmetry parameter, η, were performed. These parameters were calculated by using the GIAO method. The results show solvent-induced shielding variation is more strongly related to the intensity of the solvent reaction field rather than on the change of molecular geometry induced by the solvent.

Keywords: Pyrazole; Pyrazoline; NMR shielding; Solvent effects

INTRODUCTION

Pyrazole, any of a class of organic compounds of the heterocyclic series characterized by a ring structure composed of three carbon atoms and two nitrogen atoms in adjacent position. The simplest member of the Pyrazole family is Pyrazole itself, a compound with molecular formula $C_3H_4N_2$.The Pyrazole compounds are not known to occur in nature, they are usually prepared by the reaction of hydrazine's with 1,3-diketones. Pyrazole compounds have played an important role in many biological systems and used as a antibiotic, anticancer drugs.

Pyrazoline is a five member heterocyclic having two adjacent nitrogen atoms within the ring. It has only one double bond, a compound with molecular formula $C_3H_6N_2$. The Pyrazoline compounds are well known for their wide range of biological applications such as a fluorescent brightening agent, antimicrobial, antitubercular, antiviral, antiHIV, molluscicidal and cerebroprotective properties [1-6].

We perform a full geometrical, energetical, nuclear magnetic resonance and vibrational frequencies analysis of Pyrazole and Pyrazoline molecules with different basis set to elucidate the effect of

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site specific of these molecules. The aim of this study were to investigate the NMR shielding parameters (ppm), isotropic and anisotropic effects of hydrogen bond on shielding at different conditions (solvent) and examine the effect of dielectric constants on shielding of Pyrazole and Pyrazoline molecules.

COMPUTATIONAL METHODS

Geometries

In this investigation, the Quantum chemical study was carried out by applying Gussian 03, software package [31]. First, geometries of Pyrazole and Pyrazoline molecules were full optimized at B3LYP/6-31G and B3LYP/6-31+G (d) levels of theory in the gas phase. The minimum energy was obtained to basis set B3LYP/6-31+G (d) level. Moreover, vibrational frequencies were calculated in gas phase on the optimized geometries at the same level of theory to obtain the nature of stationary points as true minima. Then, NMR calculations were applied to the optimized structures to achieve σ_{Iso}, (σIsotropic (ppm)), σ_{Aniso}, (σAnisotropic (ppm)), anisotropic magnetic shielding tensor, $\Delta\sigma$, chemical shift, δ, total atomic charge and asymmetry parameter, η. To obtain an estimation of the solution effects, Molecular orbital calculations were also conducted on the gas phase optimized geometries using a Self-Consistent Reaction-Field (SCRF) model. Therefore all calculations were repeated in various solvents such as Water (ε=78.39), Methanol (ε=32.63) and Ethanol (ε=24.55).

RESULTS AND DISCUSSION

In first step, we found the Pyrazole and Pyrazoline to be stable in the optimized gas phase at B3lyp/6-31G+ (d) level. The optimized B3LYP/6-31+G (d) structures for the Pyrazole and Pyrazoline molecules are displayed in Fig.1 (a-b). Also the calculation results relative energy (kcal mol^{-1}) and dipole moments (Debye) in gas phase are shown in Table1. According to this result, the minimum energies were related to basis set 6-31+G (d) level. Then, a Self Consistent Reaction-Field (SCRF=PCM) model with three solvents including: (Water, Methanol and Ethanol) were used in these calculations. A quantum mechanical analysis of the solvent effects on the energies and dipole moments of Pyrazole and Pyrazoline molecules are presented in Table2. Regular alternations were observed concerning energy versus dielectric constant. With increasing dielectric constant, ε, of the solvents, the calculated energies of Pyrazole and Pyrazoline decrease. The plot of μ versus $1/\varepsilon$ in both gas and in solution is shown in Fig.2, with increasing dielectric constant,ε, of solvents, the dipole moment,μ, of Pyrazole and Pyrazoline molecules increase.

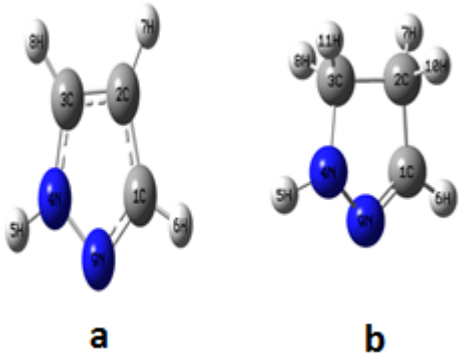

Fig.1. Optimized geometries of the Pyrazole (a) and Pyrazoline (b) obtained at the B3LYP/6-31+G (d) level.

Therefore, here the basis set of 6-31+G (d) was selected for determining NMR parameters such as σisotropic, σanisotropic, anisotropic magnetic

shielding tensor, Δσ, chemical shift ,δ, total atomic charge and asymmetry parameter, η, for all atoms of Pyrazole and Pyrazoline molecules in both gas and in solution at GIAO method by using NMR and Molecular orbital calculations. These parameters are shown in Table3 and 4. At present, we considered these parameters.

Nuclear Magnetic Resonance analysis

Table 3 displays the calculated relative $\sigma_{Iso,}$ (σIsotropic (ppm)), σ_{Aniso} (σAnisotropic (ppm)), anisotropic magnetic shielding tensor, Δσ, chemical shift, δ, total atomic charge and asymmetry parameter, η, in both gas phase and in solution, for Pyrazole molecule at GIAO method. In addition the plots of calculated relative anisotropic magnetic shielding tensor,Δσ, chemical shift, δ, total atomic charge and asymmetry parameter, η, versus the atomic number are drown in Figs. 2a-d respectively.

The result in Fig.3a show anisotropic magnetic shielding tensor, Δσ, the 9N nucleus has maximum value in gas phase and solution. Moreover, with increasing dielectric constant, ε, of solvent, the, Δσ, value at the site of 9N decreases. In addition, Fig.3d show asymmetry parameters, η, of 9N is largest amount. In this regard, it seems that the NMR, Δσ, η, parameters at the site of 9N nucleus are significantly influenced by intermolecular hydrogen-bonding interactions. As pointed in Table 3, 9N nucleus has smallest negative σ_{Iso}, and has largest positive σ_{Aniso} value and the 8H nucleus has smallest, σ_{Aniso}, but 2C nucleus has largest, σ_{Iso}, values. Since, the result from Table 3 show, the 8H nucleus has minimum, Δσ, value in gas phase and solution and with increasing dielectric constant,ε, of solvent the,Δσ, value decreases. Fig. 3c show total atomic charge for 4N nucleus is minimum meaning 4N nucleus has maximum electron shielding. Since, 5H nucleus has maximum total atomic charge in both gas phase and in solution, meaning 5H nucleus is diamagnetic shielding terms. Fig.3b show the 2C nucleus has the largest but 9N nucleus has the smallest chemical shift, δ, constants among and other atoms, respectively.

Table 4 displays the calculated relative σ_{Iso}, (σIsotropic (ppm)), σ_{Aniso}, (σAnisotropic (ppm)), anisotropic magnetic shielding tensor, Δσ, chemical shift, δ, total atomic charge and asymmetry parameters, η, in both gas phase and in solution, for Pyrazoline molecule at GIAO method. In addition the plots of calculated relative anisotropic magnetic shielding tensor, Δσ, chemical shift, δ, total atomic charge and asymmetry parameters, η, versus the atomic number are drown in Fig.4a-d respectively.

The result in Fig.4a show the 9N nucleus has largest amounts of magnetic shielding tensor, Δσ, in gas phase and solution. In addition, Fig.4a show, with increasing dielectric constant, ε, of solvent, the, Δσ, value at the site of 9N decreases. Moreover, Fig.4d show the 9N nucleus has largest amounts of asymmetry parameters, η, in gas phase and solution. It can be said, the NMR,Δσ, η, parameters at the site of 9N nucleus are significantly influenced by intermolecular hydrogen-bonding interactions. As pointed in Table 4, the 9N nucleus has smallest negative σ_{Iso}, and has largest positive σ_{Aniso}, value and the 6H nucleus has smallest ,σ_{Aniso}, but 2C nucleus has largest σ_{Iso} values. Since, the result from Fig. 4a show, the 6H nucleus has minimum, Δσ, value in gas phase and solution and with increasing dielectric constant, ε, of solvent the, Δσ, value decreases. Fig. 4c show total atomic charge for 4N nucleus is minimum meaning 4N

nucleus has maximum electron shielding. Since, 5H nucleus has maximum total atomic charge in both gas phase and solution, meaning 5H nucleus is diamagnetic shielding terms. Fig. 4b show the 2C nucleus has the largest but 9N nucleus has the smallest chemical shift,δ, constants among and other atoms, respectively.

Table 1. Calculated result relative energy (kcal mol^{-1}) and dipole moments (Debye) of the Pyrazole and Pyrazoline in the gas phase

E(kcal mol^{-1})		
Basis set	Pyrazole	Pyrazoline
6-31G	-141892.713	-142637.435
6-31+G(d)	-141948.219	142692.014
μ(Debye)		
6-31G	2.3818	2.5073
6-31+G(d)	2.4152	2.5358

Table 2. The solvent effects on the stability energies and dipole moments of Pyrazole and Pyrazoline molecules as a function of dielectric constant by using B3LYP/6-31+G (d) method

E(kcal mol^{-1})			
Solvents	ε	Pyrazole	Pyrazoline
Water	78.39	-141958.728	-142700.212
Methanol	32.63	-141958.371	-142699.868
Ethanol	24.55	-141958.171	-142699.701
μ(Debye)			
Water	78.39	3.4123	3.4842
Methanol	32.63	3.3770	3.4509
Ethanol	24.55	3.3579	3.4330

CONCLUSIONS

The solvent effects on the stability energies (kcal mol^{-1}) and dipole moments (Debye) shows, with increasing dielectric constant from gas phase to water, the stability and dipole moment of Pyrazole and Pyrazoline increases.

The 9N nucleus for Pyrazole has maximum anisotropic chemical shift tensor,Δσ, but the quantity in the 8H is minimum. Moreover, the 9N nucleus for Pyrazole has largest amount asymmetry parameters,η, in both gas phase and solution. In this regard, it seems that the NMR,Δσ,η, values at the sits of 4N and9N for Pyrazole as well as 2C and 3C are significantly influenced by intermolecular hydrogen –bonding interactions.

The 9N nucleus for Pyrazoline has maximum anisotropic chemical shift tensor,Δσ, but the quantity in the 6H is minimum. Moreover, the 9N nucleus for Pyrazoline has largest amount asymmetry parameters,η, in both gas phase and solution. In this regard, it seems that the NMR, Δσ, η, values at the sits of 4N and 9N for Pyrazoline as well as 1C are significantly influenced by intermolecular hydrogen – bonding interactions.

With this information, we can discuss the effect of variable solvent on Pyrazole and Pyrazoline, and whenever special reaction must be done.

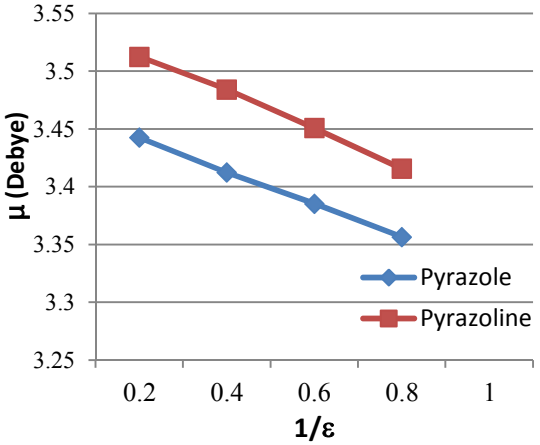

Fig. 2. Plot of the μ (Debye) versus the 1/ε, obtained from the B3LYP/6-31+G (d) calculation for Pyrazole and Pyrazoline Molecules.

Table 3. Calculated result NMR parameters of Pyrazole in gas phase and various solvents at GIAO method

GIAO						
Atomic number	σ_{Iso} (ppm)	σ_{Aniso} (ppm)	$\Delta\sigma$ (ppm)	δ (ppm)	Charge (a.u)	η (ppm)
			Gas phase			
1C	56.4821	127.6690	127.6695	56.4821	-0.219158	0.559753
2C	90.6732	115.9069	115.9073	90.6732	-0.036496	0.644832
3C	71.2251	120.0527	120.0529	71.2251	-0.213232	0.485962
4N	63.5774	120.9012	120.9018	63.5774	-0.326992	0.957786
5H	23.0849	4.8788	4.8793	23.0848	0.414353	0.416921
6H	24.5597	2.8368	2.8375	23.8931	0.189570	0.435678
7H	25.9436	2.0805	2.0812	25.9839	0.189323	0.486115
8H	24.9119	2.0721	2.0727	24.9118	0.202414	0.452889
9N	-44.1447	349.1063	349.1068	-44.1446	-0.199782	0.974508
			Water			
1C	55.8641	129.7155	129.7158	55.8409	0.001226	0.514783
2C	90.7129	116.6711	116.6716	90.7129	0.130406	0.624761
3C	67.0264	128.2725	128.2729	67.0263	0.035551	0.542614
4N	55.9645	140.1388	140.1393	55.9643	0.169268	0.923427
5H	21.4487	5.4527	5.4535	21.4663	0.000000	0.301452
6H	24.2445	2.6611	2.6616	24.2444	0.000000	0.392876
7H	25.5282	1.8879	1.9475	25.5282	0.000000	0.385149
8H	24.2400	1.9902	1.9915	24.2399	0.000000	0.401529
9N	-28.8169	325.5441	325.5458	-28.8169	-0.336451	0.934269
			Methanol			
1C	55.8786	129.6569	129.6575	55.9032	-0.226211	0.531069
2C	90.7235	116.6274	116.6282	90.7235	-0.096411	0.593957
3C	67.1830	127.9830	127.9837	67.1830	-0.219265	0.524183
4N	56.2383	139.5316	139.5328	56.2382	-0.331982	0.935741
5H	21.5084	5.4308	5.4326	21.5084	-0.498543	0.471583
6H	24.2557	2.6660	2.6667	24.2556	0.226285	0.415836
7H	25.5430	1.8932	1.8935	25.5430	0.227685	0.452173
8H	24.2641	1.9916	1.9924	24.2641	0.253155	0.392587
9N	-29.3214	326.3105	326.3125	-29.3214	-0.331800	0.968721
			Ethanol			
1C	55.8901	129.6365	129.6373	55.9400	-0.226022	0.545698
2C	90.7340	116.6011	116.6028	90.7340	-0.095289	0.584723
3C	67.2709	127.8271	127.8276	67.2709	-0.219152	0.522649
4N	56.3975	139.2121	139.2127	56.3975	-0.331744	0.951593
5H	21.5433	5.4157	5.4164	21.6597	0.496867	0.297564
6H	24.2617	2.6698	2.6705	24.2617	0.225574	0.419574
7H	25.5525	1.8957	1.8963	25.5525	0.226917	0.483982
8H	24.278	1.9942	1.9947	24.2786	0.252155	0.425798
9N	-29.6108	326.7219	326.7228	-29.6108	-0.329305	0.971589

Table 4. Calculated result NMR parameters of Pyrazoline in gas phase and various solvents at GIAO method

GIAO						
Atomic number	σ_{Iso} (ppm)	σ_{Aniso} (ppm)	$\Delta\sigma$ (ppm)	δ (ppm)	Charge (a.u)	η (ppm)
1C	56.6983	97.8358	97.8469	56.6982	-0.079514	0.559562
2C	155.2846	31.7740	31.7746	155.2845	-0.440059	0.644837
3C	142.4775	47.7609	47.7615	142.4774	-0.367410	0.485974
4N	120.1349	157.7009	157.7411	120.1348	-0.450488	0.957792
5H	27.1936	7.1356	7.1523	27.1935	0.388310	0.496135
6H	25.6712	1.1320	1.1325	25.6712	0.193003	0.435684
7H	29.5335	7.3319	7.3328	29.5334	0.212527	0.486126
8H	28.9120	8.9130	8.9136	28.9120	0.190131	0.452897
9N	-102.3235	395.9083	395.9096	-102.3234	-0.067674	0.974514
10H	29.4073	8.8168	8.8173	29.4072	0.217874	0.491586
11H	28.5800	6.6817	6.6824	28.5799	0.203301	0.496328
			Water			
1C	48.9093	112.2492	112.2498	48.9093	-0.063967	0.514785
2C	156.0748	31.2268	31.2275	156.0747	-0.463180	0.624769
3C	142.1838	49.6424	49.6428	142.1837	-0.357636	0.542631
4N	120.6247	142.2471	142.2476	120.6247	-0.545516	0.923432
5H	26.0151	7.8121	7.8125	26.0152	0.454422	0.401458
6H	25.0345	0.9752	0.9764	25.0344	0.233565	0.342885
7H	29.3397	7.5214	7.5223	29.3397	0.234158	0.365267
8H	28.9637	9.0280	9.0284	28.9637	0.209889	0.401536
9N	-81.0390	375.6323	375.6329	-81.0389	-0.154430	0.934968
10H	29.3627	8.9124	8.9130	29.3627	0.234921	0.461582
11H	28.5949	6.7615	6.7618	28.5949	0.217773	0.465218
			Methanol			
1C	49.2111	111.7171	111.7175	49.2110	-0.064273	0.531172
2C	156.0946	31.1750	31.1758	156.0945	-0.463111	0.614167
3C	142.1803	49.5863	49.5872	142.1802	-0.357974	0.526381
4N	120.6193	142.1374	142.1375	120.6193	-0.541692	0.936812
5H	26.0629	7.7894	7.7896	26.0629	0.452011	0.463175
6H	25.0579	0.9749	0.9751	25.0579	0.232058	0.412693
7H	29.3509	7.5160	7.5162	29.3509	0.233378	0.408952
8H	28.9678	9.0256	9.0264	28.9677	0.209181	0.435891
9N	-81.5440	376.5433	376.5436	-81.5440	-0.151413	0.953874
10H	29.3663	8.9144	8.9148	29.3663	0.234462	0.478216
11H	28.5961	6.7554	6.7559	28.5962	0.217373	0.472583
			Ethanol			
1C	49.3448	111.4953	111.4958	49.3447	-0.064141	0.548135
2C	156.1083	31.1322	31.1325	156.1082	-0.463259	0.604785
3C	142.1712	49.5502	49.5514	142.1710	-0.358068	0.514362
4N	120.5698	142.1808	142.1814	120.5697	-0.539605	0.945215
5H	26.0874	7.7716	7.7720	26.0873	0.450660	0.471939
6H	25.0694	0.9735	0.9814	25.0693	0.231262	0.428163
7H	29.3574	7.5145	7.5152	29.3574	0.232984	0.441982
8H	28.9700	9.0230	9.0241	28.9699	0.208798	0.471158
9N	-81.8640	376.9883	376.9887	-81.8639	-0.149982	0.965934
10H	29.3681	8.9128	8.9136	29.3680	0.234197	0.493152
11H	28.5973	6.7512	6.7518	28.5972	0.217153	0.489631

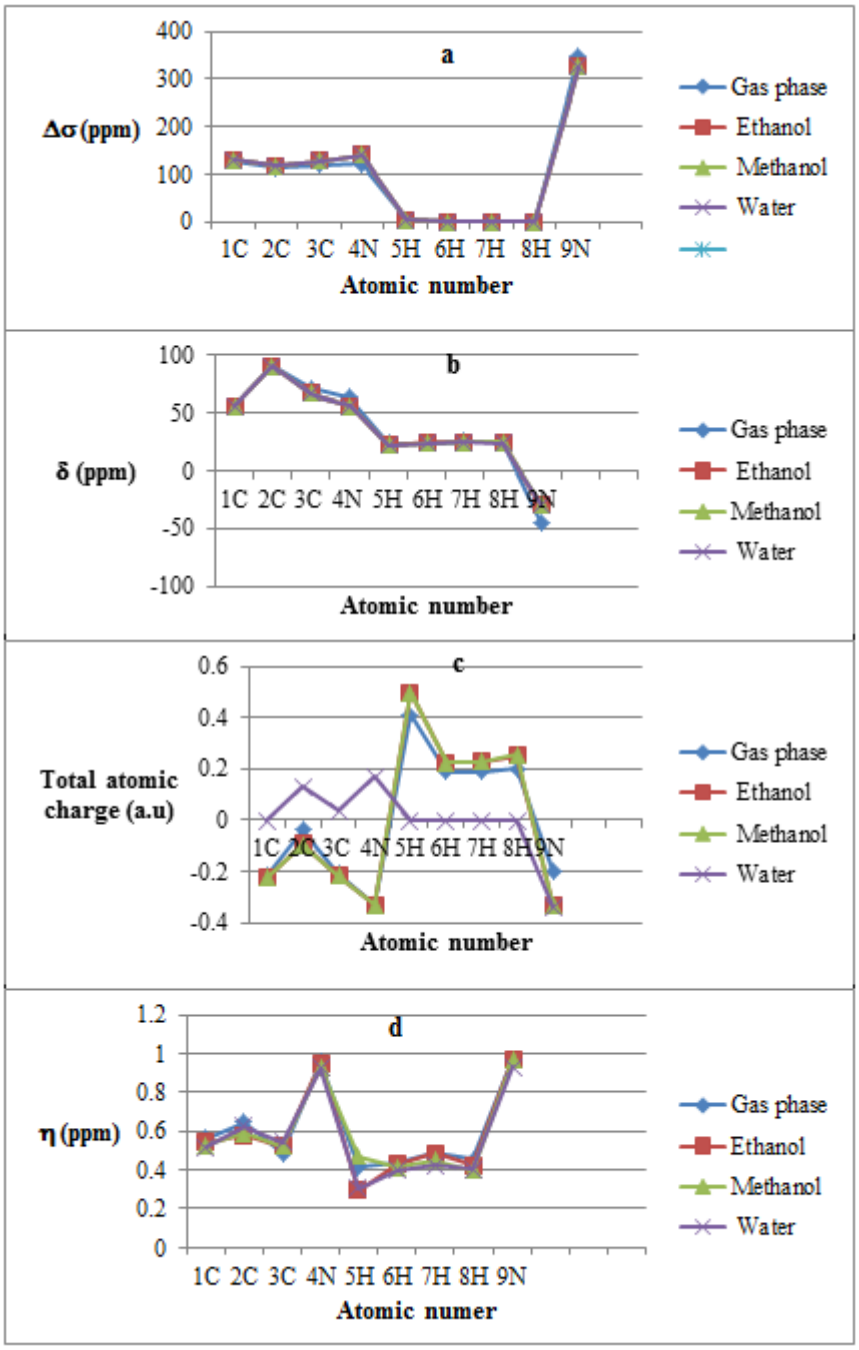

Fig. 3. Plots of NMR parameters such as a)Δσ (ppm), b) δ (ppm), c) total atomic charge (a.u) and d) η (ppm) versus atomic number of Pyrazole in gas phase and various solvents at GIAO method.

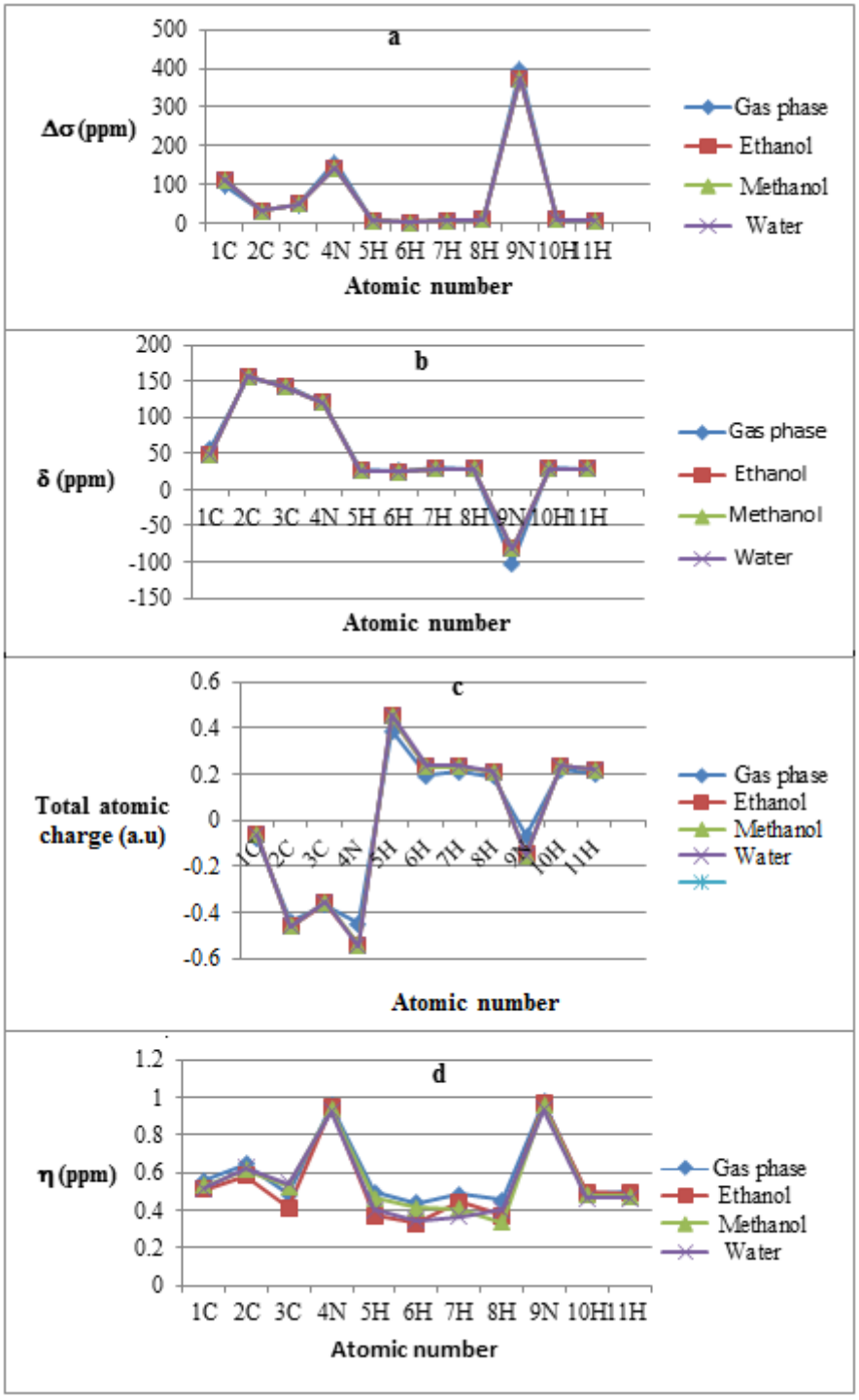

Fig. 4. Plots of NMR parameters such as a) Δσ (ppm), b) δ (ppm), c) total atomic charge (a.u) and d) η (ppm) versus atomic number of Pyrazoline in gas phase and various solvents at GIAO method.

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