Theoretical NMR investigation of pyrazol and substituted pyrazoles, DNMR and ^{1}H spin-lattice relaxation times

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Abstract

NMR spectra of pyrazole and substituted pyrazoles were theoretically investigation by ab initio at MP2 theory level using 6-31G(d,p) basis sets by TNDO method and were experimentally measured in solutions, and related to the structure . DNMR have been studied in the temperature range -40 to 60 ℃, and ^{1}H spin-lattice relaxation times (T_1) were determined by inversion method using 180^o-τ-90^o sequence and discussed in term of the structure and molecular motions .

Keywords : NMR theoretical investigation, ab initio MP2/TNDO,DNMR, spin-lattice relaxation times, pyrazole, substituted pyrazoles.

ملخص

بحُثت أطياف الرنين النووي المغناطيسي البروتوني للبايرازول وبعض مشتقاته نظرياً بواسطة حسابات ab initio عند المستوى النظري MP2 ومجموعة الدوال 6-31G(d,p) وبطرقة TNDO وتم قياس الأطياف عملياً في المحاليل وفسرت على أساس التركيب , وتم كذلك دراسة الرنين النووي المغناطيسي الديناميكي (DNMR) في المدى الحراري -40 الى 60 م^o وعينت أزمنة الاسترخاء الطولي بطريقة الانقلاب باستخدام التعاقب 180^o-τ-90^o وتم مناقشتها حسب التركيب والحركة الجزيئية .

Introduction

Pyrazole is an aromatic heterocyclic compound containing two adjacent bonded nitrogen atoms . It is related to many compounds such as isoxazole, isothiazole, thiazole, oxazole and imidazole[1]. pyrazole and derivatives have wide spread applications in the fields of medicine[2-9] and industry[10] , pyrazole molecule is stabilized by resonance structure and posses amphoteric property[11-12]. However, it undergoes a cyclic tautomeric by exchange of the hydrogen atom between the nitrogen atoms of the aromatic ring[13-14]. We have previously studied theoretically the structure, IR frequencies and some physical properties of these compounds . Also, we have determined the structure of some of these compounds by X-ray diffraction[15].The aim of the present work was devoted to investigate theoretically NMR spectra of these compounds and study their DNMR and spin-lattice relaxation times in solutions .

1. Experimental

1.1 Preparations

The studied compounds, as reported previously, were prepared by reaction of corresponding β –diketones with hydrazine and substituted hydrazine[16,17] and characterized by MP and CHN analysis .

1.2 NMR spectra

^{1}H NMR spectra for studied compounds were recorded on a Bruker FT-NMR spectrometer operating at 500.13 MHz in CDCl3 or DMSO using TMS as interval standard for pyrazole and 3,5-dimethylpyrazole. All the measurements have been carried out at Tehran University.

1.3 DNMR

^1H spectra were measured in the temperature range -40 to 60 °C for all compounds in CDCl3.

1.4 Spin-Lattice relaxation times (T_1)

Spin-Lattice relaxation times (T_1) were determined for S_1,S_2 and S_4 compounds at 40°C in CDCl3 by inversion method using 180^o-τ -90^o sequence.

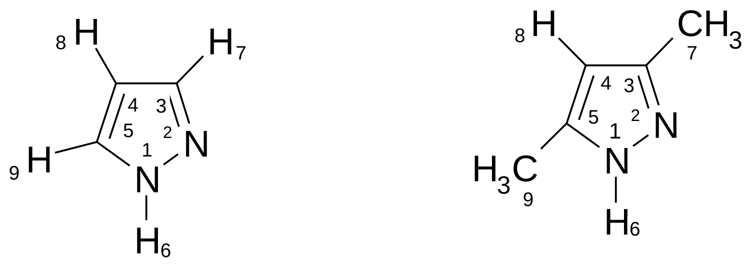
2. Computational

ab initio MP2 method was used at 6-31G(d,p) basis set for geometry optimization, there chemical shifts were calculated by TNDO method using HyperChem software.

3. Results and discussion

3.1 NMR spectra

Experimental and theoretically calculated proton chemical shifts using TNDO method for compounds S_1 and S_2 are listed in Table 1. The compounds are represented by the following numbering structural formula :-



S_1 S_2

Fig.1 Structural formula of $S_1$and S_2 with numbering atoms.

Table 1 Experimental and theoretically calculated chemical shifts for S_1 and S_2 compounds (in ppm) using TNDO method.

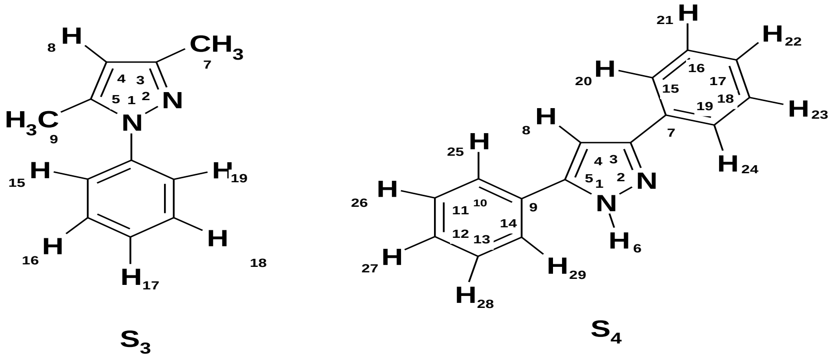
Compound symbol	Experimental chemical shift	Theoretical chemical shift	Proton number
S_1	11.844	12.900	H_6
	7.655	7.422	H_7
	6.369	6.344	H_8
	7.655	7.422	H_9
S_2	12.251	11.437	H_6
	2.296	2.215	$^7CH_3$
	5.826	7.262	H_8
	2.296	2.355	$^9CH_3$

^1H NMR spectrum of S_1 shows two signals at 6.369 and 7.657 ppm. The first signal is triplet with coupling constant 2 Hz and intensity equivalents to are proton. Therefore, it can be assigned to the proton H_8. The second signal which appears as a doublet with intensity equivalents to two protons is arised from H_7 and H_9 protons. This observation indicates that the two protons are accidently chemically equivalent, at 22.3 ℃ . However, NH group gives, a signal at 12.900 ppm. On the other hand proton H_9 is not showing coupling with NH, probably due to relatively fast exchange of NH proton.

From Table 1, substitution of CH_3 groups at positions 7 and 9 causes downfield shift of H_8 according to theoretical calculations. However, the measured spectrum of S_1 and S_2 show broad signals at 11.844 and 12.251 ppm respectively , the brooding is due to quadruple interaction of H_6 with ^{14}N nucleus. In general the calculated chemical shifts are in good agreement with the theoretical.

From the data (Table 1) the two methyl groups are equivalent in S_2 but become not equivalent when H_6 is substituted by phenyl group us in S_3 compound (Table 2), this is due the effect of the aromatic ring which shifted CH_3 to down field (exp. 2.641 ppm). In addition substitution of p-Toluene sulphonyl group at 6 position shifted H_7 and H_9 protons to up field (7.355 ppm) as in S_5 (Table 3).

The experimental and theoretical NMR data by TNDO method for S_3 and S_4 compounds are shown in Table 2, the compounds are represented by numbered structural formula :-



S_3 S_4

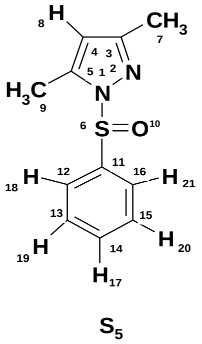
Fig. 2 structural formula of S_3 and S_4 compounds

Table 2 Experimental and theoretical NMR data by TNDO method for S_3 and S_4 compounds

Compound symbol	Experimental chemical shift	Theoretical chemical shift	Proton number
S_3	2.367	2.142	$^7CH_3$
	6.298	7.503	H_8
	2.641	2.583	$^9CH_3$
	7.583	6.897	H_{15}
	7.583	6.897	H_{19}
	7.533	6.633	H_{16}
	7.533	6.633	H_{18}
	7.583	6.897	H_{17}
S_4	13.576	11.847	H_6
	6.881	6.756	H_8
	7.760	6.981	H_{20},H_{24}
	6.981	7.760	H_{21},H_{23}
	6.834	7.386	H_{22}
	6.981	7.760	H_{25},H_{29}
	6.972	7.460	H_{26},H_{28}
	6.834	7.381	H_{27}

In general H_8 undergoes up field shift by the two methyl groups (as in S_2) and p-Toluene sulphonyl group (as in S_5) whereas it is shifted to down field as in S_4 by the two phenyl groups at 7 and 9 positions.

Table 3 Experimental and theoretical NMR data
(δ ppm) calculation by TNDO method for S_5 compound.



S_5

Experimental chemical shift	Theoretical chemical shift	Proton number
7.335	6.371	H_7
6.405	5.882	H_8
7.335	8.949	H_9
2.434	1.429	$^{17}CH3$
8.124	6.879	H_{21},H_{18}
7.920	5.670	H_{19},H_{20}

3.2 ^{14}N NMR

^{14}N NMR spectra for S_1 and S_2 compounds were measured in $CDCl_3$ at 27 ℃ using CH_3NO_2 as internal reference. The spectra showed a very broad signal at -146.5 and -143.4 ppm for S_1 and S_2 respectively. The broadness of the signal is due to quadruple relaxation of the ^{14}N and proton exchange. However, the appearance of only one broad signal suggests that the two nitrogen atoms almost have identical chemical environments.

3.3 DNMR

^{1}H NMR spectra for pyrazole (S_1), 3,5-dimethylpyrazole (S_2) and 3,5-diphenylpyrazol in $CDCl_3$ in the temperature range -37 to 60 ℃ using TMS as have been measured. The temperature interval was 10 ℃ .

The S_1 spectrum at different temperatures with is shown in Fig. 1. The two signals at 6.369 and 7.657 ppm are easily assigned to proton 8 and H_7,H_9 protons respectively in pyrazole molecule. The N-H signal is shifted to high field with increasing temperature (Fig. 1). This can be explained in term of breaking of NH···N Hydrogen bonding as the temperature increases. The expansion spectrum (Fig. 2) shows that the signal at 6.369 ppm is triplet, with coupling constant 2 Hz, this means that the two protons, 7 and 9 are accidently chemically equivalent. The signal of protons 7 and 9 appears as doublet due to coupling with H_8 proton. However, the spectrum of S_1 measured below 10 ℃ showed relatively broad signal. This observation can be explained in term of slaw.

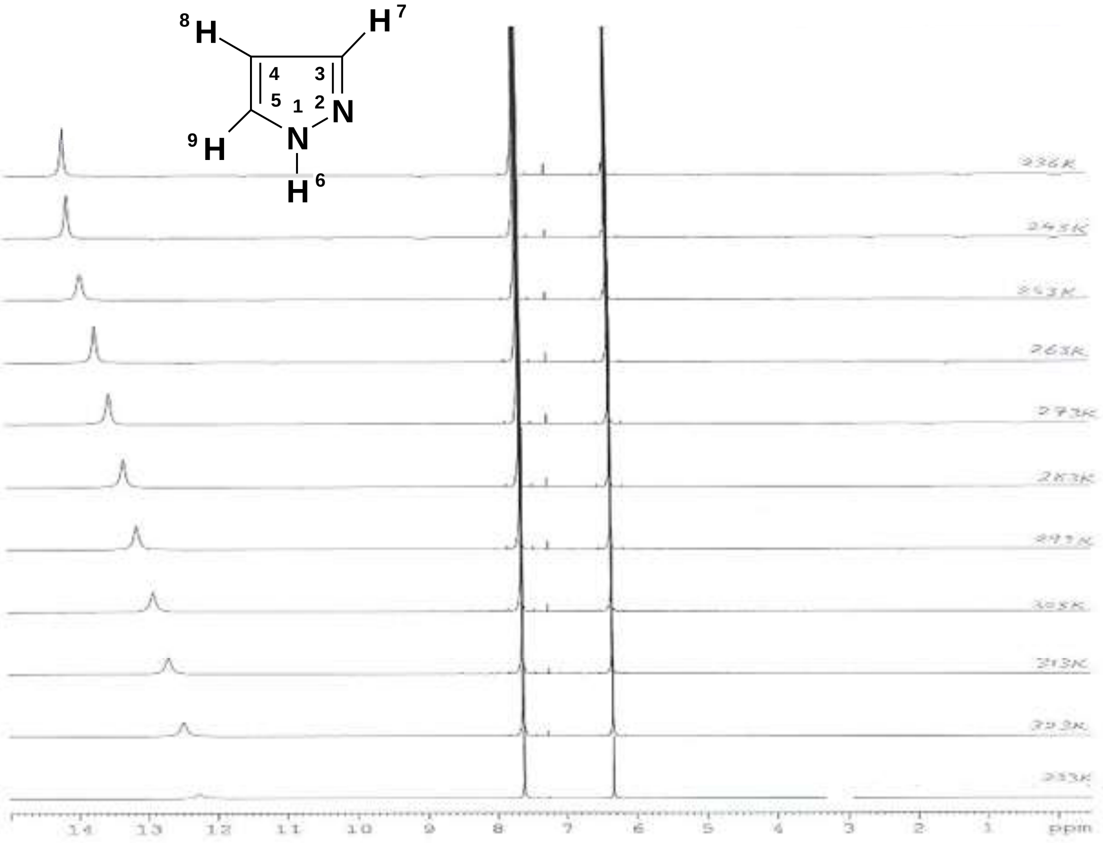


Fig. 3 ^{1}H NMR spectrum of S_1 at different temperatures

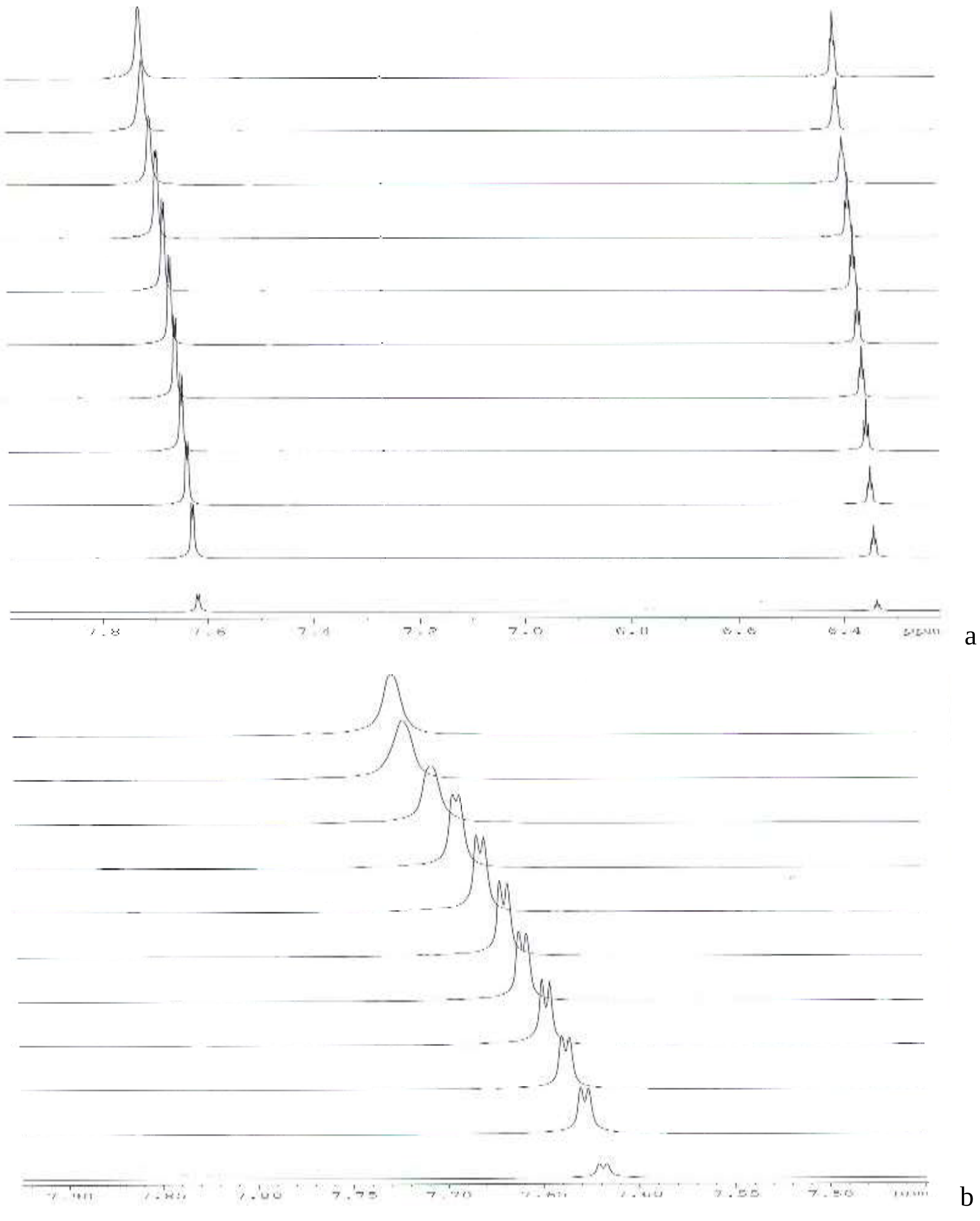


Fig. 4 ^{1}H NMR spectrum of S_1 with expansion at different temperatures

a) 6.4 - 7.8 ppm
b) 7.5 - 7.9 ppm

Rate of molecules orientation about the molecular axis containing C-H_8 bond[18,19,20].
The variation of NH chemical shift with temperature is shown in Fig. 3. The relation is almost linear and can be used as temperatures monitor.

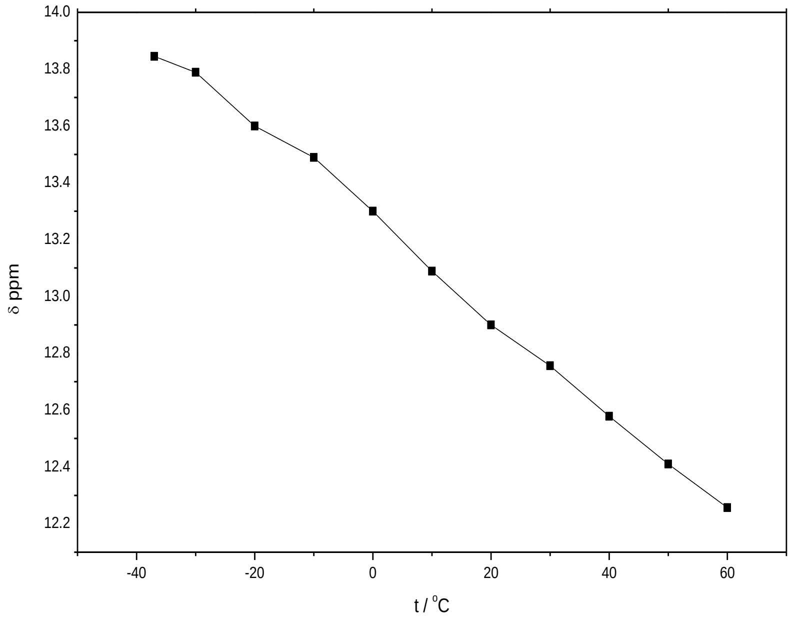
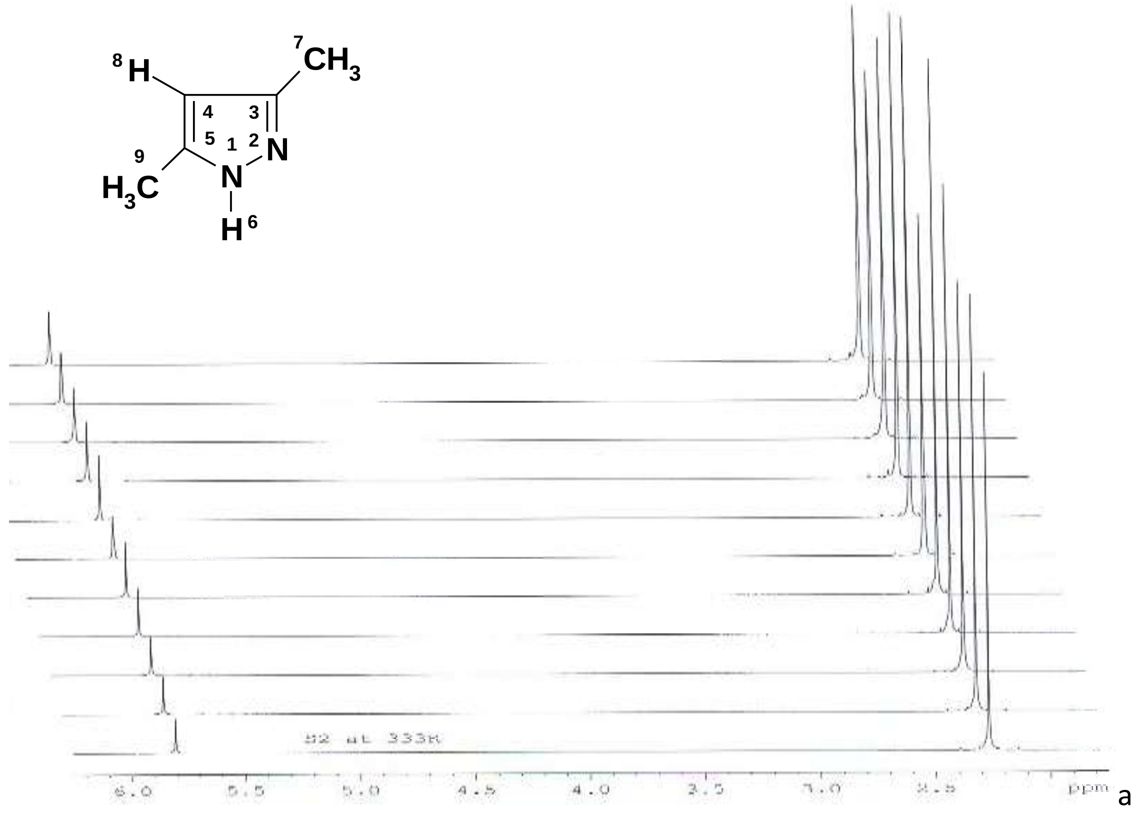


Fig. 5 variation of NH chemical shift (S_1) with temperatures.

DNMR spectrum of S_2 is shown in Fig. 4. It consists of three signals ; δ 2.296 ppm, 2 CH_3 (6H); δ 5.826 ppm, C=CH (1H); δ 12.251 ppm, NH (1H), which is in consistence with the structure; The variation of NH chemical shift (in S_2) with temperature is shown in Fig. 5. The chemical shift, as in S_1, shifts to up field due to breaking of hydrogen bonding.



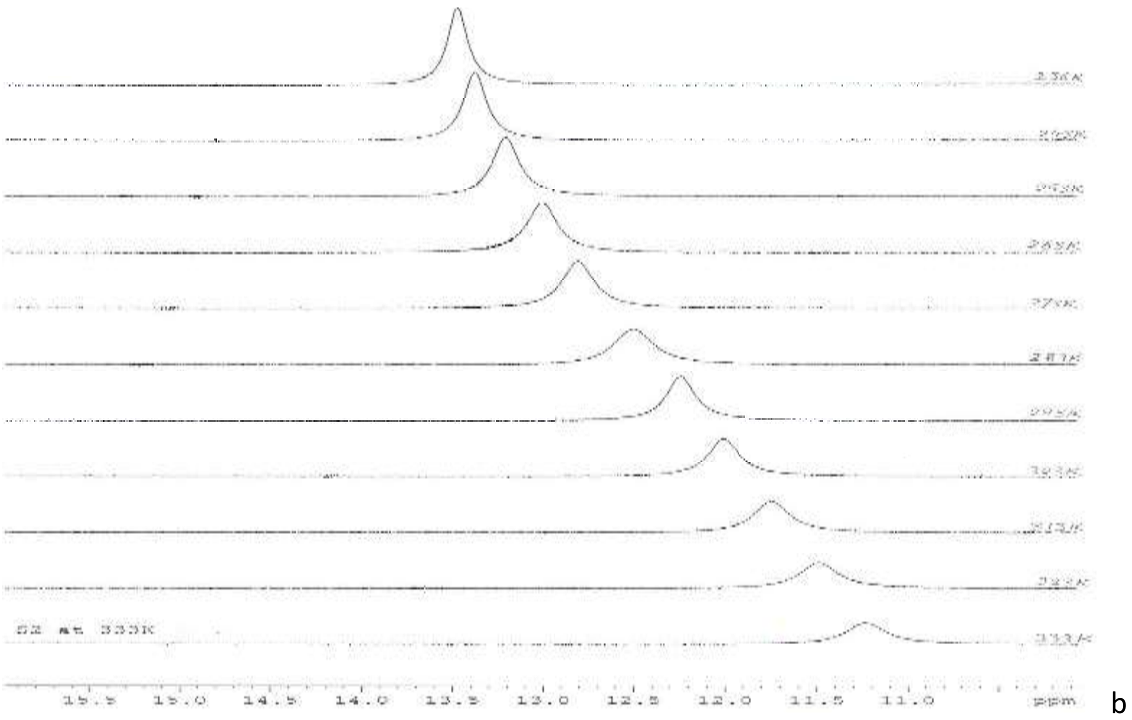


Fig. 6 Expanded DNMR of S_2.

a) 2.5 – 6.0 ppm
b) 11.0 – 15.5 ppm

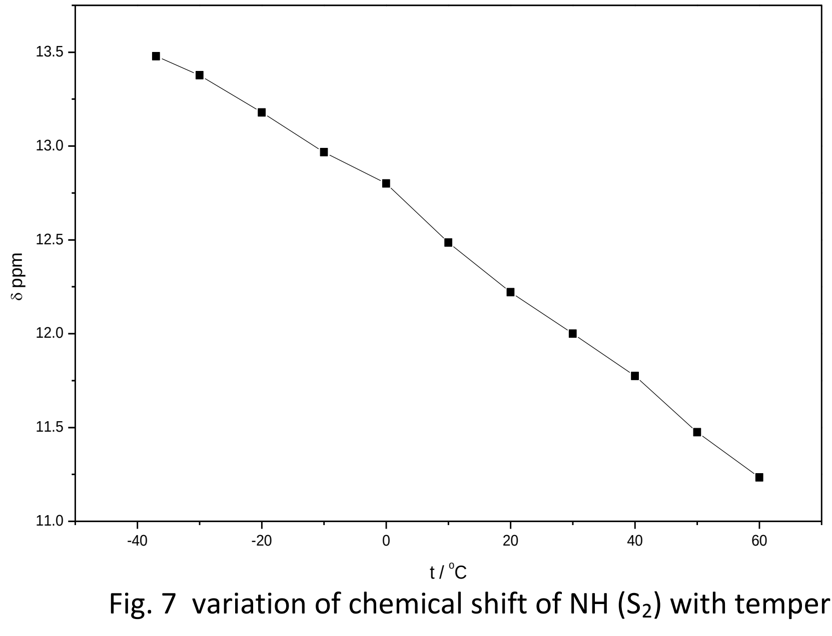


Fig. 7 variation of chemical shift of NH (S_2) with temperatures.

DNMR of S_4 is shown in Fig. 8 in the range 9.5 – 14.5 ppm. The NH broad signal is shifted to up field by increasing the temperature (Fig. 9) and be comes broader. In general NH signal is broad due to the quadruple interaction of ^{14}N nucleus with the proton when the rate of proton exchange Is slow. The electrical quadruple moment of ^{14}N induces moderately efficient spin relaxation. The NH signal is shifted to up field due to breaking of H-bonding. On the other hand the line width increases with temperature due to increase rate of proton exchange, when the rate exchange becomes very fast the proton decouples from ^{14}N nucleus and the signal becomes sharp. On the other hand the H_8 signal is unaffected by the temperature (Fig. 8).

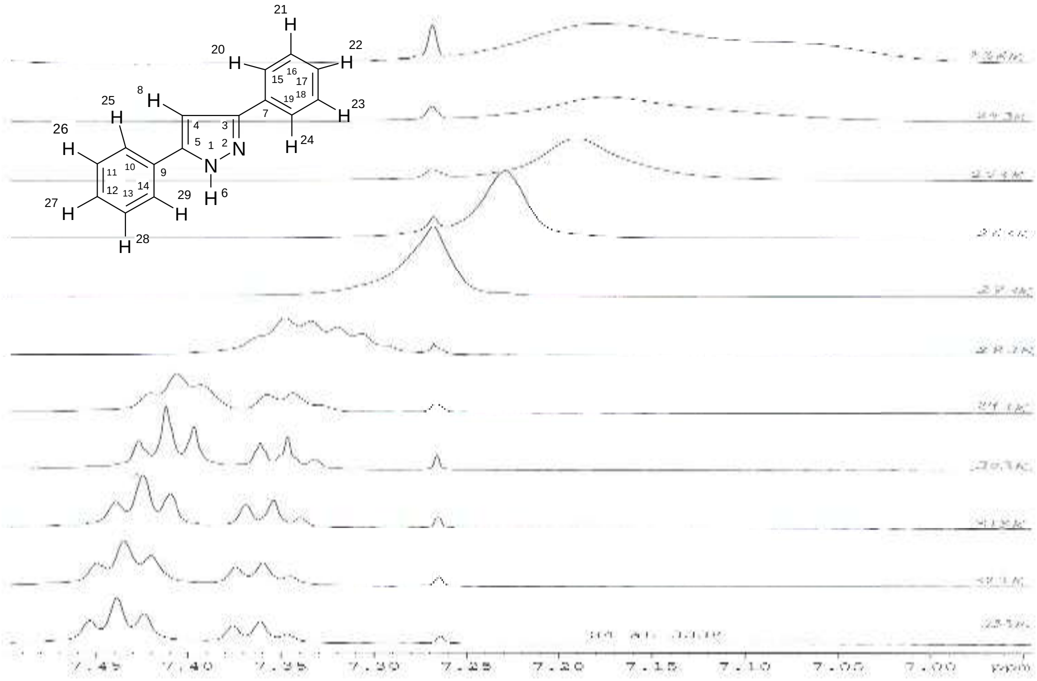


Fig. 8 DNMR of S_4 in the range 7.0 – 7.4 ppm

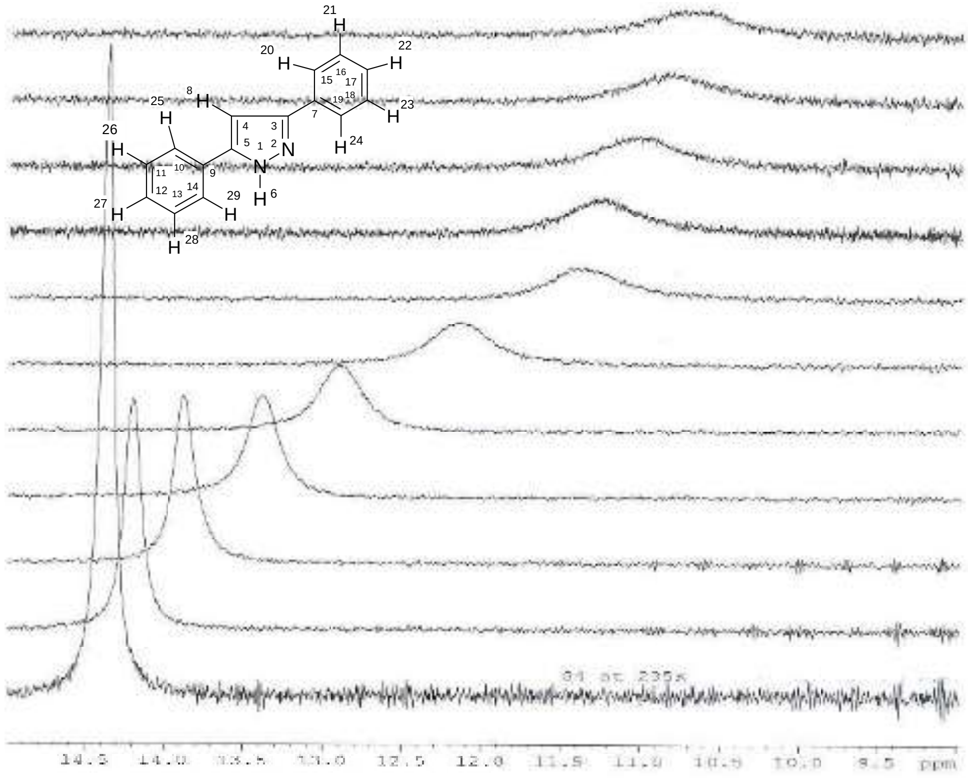


Fig. 9 Variation of NH signal of S_4 with temperature.

3.4 ^{1}H spin-lattice relaxation time (T_1)

^{1}H spin-lattice relaxation time (T_1) have been determined for S_1 , S_2 and S_4 compounds in $CDCl_3$ at 40 ℃ , using inversion recovery method, 180^o- τ- 90^o sequence. The results are shown in Fig. 10.

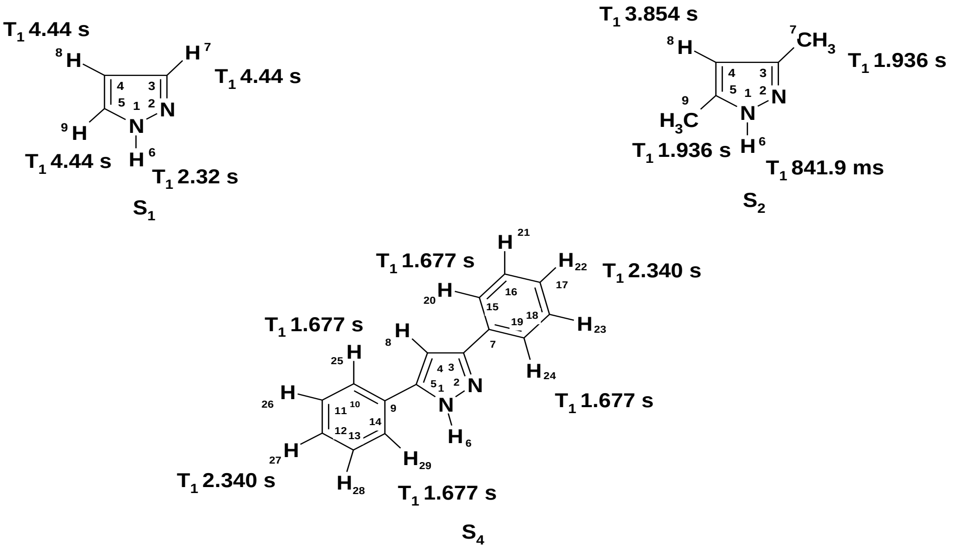


Fig. 10 T_1 values for S_1,S_2 and S_4 compounds in $CDCl_3$ at 40℃ .

It is clear that H_7 and H_9 have equal T_1 values but H_8 proton shows danger T_1. The observation indicates that the tow protons (H_7 and H_9) are identical and the molecule undergoes rotation about molecular axis containing C_4-H_8 bond which causes T_1 of H_8 to be longer. However, H_6 shows shorter T_1 (2.32 s) probably due to quadruple relaxation effect of ^{14}N. Similarly, in S_2, the two methyl groups have equal T_1 values (1.936 s) as expected, but shorter them T_1 of H_8 proton. This is due to presence of three protons on the some carbon atom which makes the dipolar interaction strong and which is modulated by reorientation of the methyl group. However, by comparing S_1 with S_2, one can conclude that the presence group increases the rate of relaxation of protons H_8 and H_6.The T_1 data of S_4 compound (Fig. 10) show that the protons in p-position in the benzene ring have longer T_1 than that in o-position, probably due to reorientation of the benzene ring about the bond connects the benzene and pyrazole rings.

4. Conclusion

The theoretically calculated chemical shifts by TNDO fro studied compounds are in agreement with the experimental. The NH signal is broad and shifted to up field with increasing temperatures. ^{1}H T_1 indicates the protons H_7 and H_9 are equivalent in pyrazole and proton H_6 has shorter T_1 due to quadruple interaction of ^{14}N.

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