



# A theoretical study of dynamic processes observed in trimethylsilyl-1*H*-pyrazoles: prototropy and silylotropy

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## Abstract

The <sup>1</sup>H, <sup>13</sup>C, <sup>15</sup>N and <sup>29</sup>Si chemical shifts of three trimethylsilyl-1*H*-pyrazoles were calculated and compared with literature results; the calculations were carried out at the GIAO/B3LYP/6–311 + +G(d,p) level resulting in a very good agreement that allows to predict with confidence the missing experimental values. The prototropic barrier of 4-trimethylsilyl-1*H*-pyrazole (**1**) as well as the silylotropic barriers of 1-trimethylsilyl-1*H*-pyrazole (**2**) and 1-trimethylsilyl-4-methyl-1*H*-pyrazole (**3**) were also calculated and the mechanism was established, the accordance with the experimental values being satisfactory.

**Keywords** Pyrazoles · Trimethylsilyl · Prototropy · Silylotropy · DFT calculations · GIAO

## 1 Introduction

Dynamic phenomena are one of the essential aspects of chemistry; some of these phenomena occur without breaking/creating bonds, such as the conformational analysis of molecules [1], while others involve the building and breaking of bonds, the most known being prototropic tautomerism [2]. These processes are studied by dynamic NMR the technique being called DNMR.

Although prototropic tautomerism is important in general organic chemistry, for instance in β-diketones [3], most results come from heterocycles [2], particularly from azoles that have a *N*-substituted nitrogen atom and a *N*-unsubstituted one. In pyrazoles (but also in triazoles and tetrazoles), these nitrogen atoms occupy contiguous positions that facilitate the transfer of the migrating atom.

Proton transfer is by far the most common process, but nonetheless other groups can also migrate, among them, silyl groups like the trimethylsilyl (TMS) [4]. In 1998, Larina et al. reported a large series of NMR data in a paper where they wrote, "*C*- and *N*-trimethylsilylazole derivatives were

studied by <sup>1</sup>H, <sup>13</sup>C and <sup>29</sup>Si NMR spectroscopy. Degenerated prototropic tautomerism of 4-trimethylsilyl-pyrazole (**1**) in methanol and the silylotropy of 1-trimethylsilyl-4-methylpyrazole (**3**) in a neat liquid were investigated for the first time" [5]. [Compound **2** was also studied in this paper (Scheme 1).]

## 2 Computational details

Density functional theory (DFT) calculations were carried out using the Becke, three-parameter, Lee, Yang and Parr (B3LYP) functional [6–8] together with the 6–311 + +G(d,p) basis set [9, 10]. Frequency calculations were carried out to verify that the structures obtained correspond to energetic minima (I=0) or to transition states (TS, I=1): see Supplementary Information for the geometries of the minima and the TS.

Absolute shieldings were calculated within the GIAO approximation [11]. Empirical equations were used to transform the <sup>1</sup>H, <sup>13</sup>C, <sup>15</sup>N and <sup>29</sup>Si absolute shieldings into chemical shifts [12–14]. All these calculations have been carried out with the Gaussian 16 program [15].

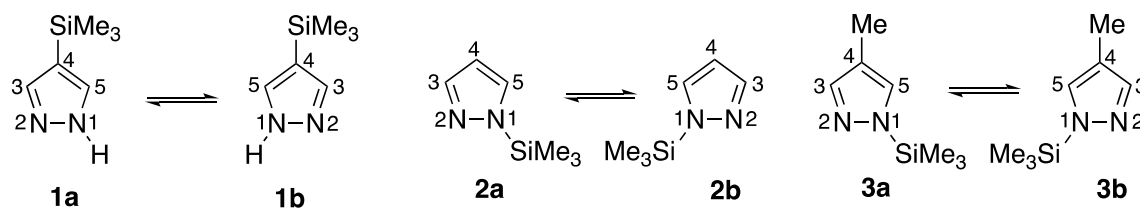
## 3 Results and discussion

There are three compounds under study:

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**Scheme 1** Three compounds under study with the atoms numbering

4-Trimethylsilyl-1*H*-pyrazole (**1**). This compound was first prepared by Birkofer [16] and studied thoroughly by him [17–20] and other authors [21–26]. (The X-ray structure of **1** has been determined [25].)

1-Trimethylsilyl-1*H*-pyrazole (**2**). Again Birkofer prepared for the first time in 1960 [27], we reported the synthesis of **2** in 1968 [28]. The subsequent syntheses were due to O'Brien [29] and to Wrackmeyer [30, 31]. We have devoted several papers to the synthesis and study of this compound [32–38].

4-Methyl-1-trimethylsilyl-1*H*-pyrazole (**3**). Reported for the first and only time by Larina et al. [5].

### 3.1 Static part

We have reported in Table 1 the calculated and experimental NMR values concerning compounds **1**, **2** and **3**. A column called "Prototropy" reports the GIAO calculated values when averaged by prototropy and silylotropy; this affects H3/H5, C3/C5 and N1/N2, for instance,  $(7.47 + 7.17)/2 = 7.32$  ppm.

**Table 1** NMR chemical shifts, all experimental data from reference<sup>5</sup> unless indicated. Mean values are given in red

Compound	GIAO	Prototropy	Exp. CDCl <sub>3</sub>	Exp. CCl <sub>4</sub>	Exp. CD <sub>3</sub> OD
<b>1</b> H1	9.06	9.06	12.97	14.58	----
H3	7.47	7.32	7.58	7.50	7.57
H5	7.17	7.32	7.58	7.50	7.57
Me ( <sup>1</sup> H, SiMe <sub>3</sub> )	0.20	0.20	0.21	0.22	0.21
C3	143.6	136.4	138.2	----	----
C4	114.5	114.5	113.6	----	----
C5	129.3	136.4	138.2	----	----
Me ( <sup>13</sup> C, SiMe <sub>3</sub> )	-1.3	-1.3	-0.2	----	----
N1	-187.2	-130.1	----	----	----
N2	-73.0	-130.1	----	----	----
Si	-15.0	-15.0	-10.35	----	----
Compound	GIAO	Silylotropy	Exp. CDCl <sub>3</sub>	Exp. neat liquid <sup>c</sup>	----
<b>2</b> H3	7.64	7.52	7.79 <sup>b</sup>	7.65	----
H4	6.19	6.19	6.33 <sup>b</sup>	6.22	----
H5	7.39	7.52	7.60 <sup>b</sup>	7.55	----
Me ( <sup>1</sup> H, SiMe <sub>3</sub> )	0.36	0.36	0.46 <sup>b</sup>	0.37	----
C3	142.7	137.2	143.1 <sup>b</sup>	143.0	----
C4	105.1	105.1	106.0 <sup>b</sup>	106.3	----
C5	131.6	137.2	132.2 <sup>b</sup>	133.6	----
Me ( <sup>13</sup> C, SiMe <sub>3</sub> )	-2.2	-2.2	-1.1 <sup>b</sup>	-0.8	----
N1	-161.0	-112.0	-162.9 <sup>a</sup> -161.1 <sup>b</sup>	----	----
N2	-63.0	-112.0	-72.5 <sup>a</sup> -71.4 <sup>b</sup>	----	----
Si	10.1	10.1	14.6 <sup>c</sup>	14.2	----
Compound	GIAO	Silylotropy	Exp. CDCl <sub>3</sub>	----	----
<b>3</b> H3	7.50	7.29	7.53	----	----
H5	7.08	7.29	7.39	----	----
Me4 ( <sup>1</sup> H, 4-Me)	2.08	2.08	2.08	----	----
Me ( <sup>1</sup> H, SiMe <sub>3</sub> )	0.32	0.32	0.40	----	----
C3	143.9	137.2	144.8	----	----
C4	117.6	117.6	116.9	----	----
C5	130.4	137.2	132.9	----	----
Me ( <sup>13</sup> C, 4-Me)	8.9	8.9	Unreported	----	----
Me ( <sup>13</sup> C, SiMe <sub>3</sub> )	-2.2	-2.2	-0.3	----	----
N1	-165.5	-113.2	----	----	----
N2	-60.8	-113.2	----	----	----
Si	9.0	9.0	13.1	----	----

<sup>a</sup>reference [39]; <sup>b</sup>reference [36]; <sup>c</sup>pure liquid: references[22, 40]

In the case of compound **1** in CD<sub>3</sub>OD at low temperature (−90 °C), only H3, H5 and SiMe<sub>3</sub> were reported to appear at 7.70, 7.56 and 0, 21 ppm, respectively.

The data of Table 1 were analyzed statistically using the calculated mean values; with regard to CDCl<sub>3</sub>, the other solvents (CCl<sub>4</sub>, CD<sub>3</sub>OD and "neat liquid") do not modify the values in a significant way; on the other hand, the NH proton of compound **1** differs significantly from the GIAO calculated value in the gas phase 9.06 vs. 12.97 and 14.58 ppm), a well-known fact [41]. In the following equation, NH variable corresponds to these differences but statistically calculated.

The resulting equation is Exp. (ppm) = (1.01 ± 0.04) GIAO (ppm) + (4.7 ± 1.6) NH (ppm),  $n=50$ ,  $R^2=0.999$ . The solvent effect on the NH is 4.7 ppm. Since the slope is 1.01, the missing experimental values of Table 1 should be very close to the calculated ones.

### 3.2 Dynamic part: barriers

We have summarized in Table 2 the experimental barriers determined by Larina et al. by DNMR for the compounds of Scheme 1 [42]. The barrier of compound **2** (**2a/2b** equilibrium) was measured by O'Brien & Hrung [29] who reported a value of 133.9 kJ mol<sup>−1</sup>. Larina et al. [22, 40, 42] using their DNMR data calculate a barrier of 96.7 kJ mol<sup>−1</sup>, using the temperature of coalescence  $T_C$  and the equation that relates the barrier energy to the temperature of coalescence:  $\Delta G_C^\ddagger = 19.12 * T_C * (10.32 + \log$

$T_C/k_C$ ), the temperature of coalescence  $T_C$  is 438 K,  $k_C = (\pi * \Delta\nu)/\sqrt{2}$ ,  $\Delta\nu = 11.6$  Hz ( $k_C = 25.8$  s<sup>−1</sup>), and consequently,  $\Delta G_C^\ddagger = 96.7$  kJ·mol<sup>−1</sup>.

It is well known that the direct proton transfer in NH-pyrazoles is forbidden resulting in very high barriers; solvent molecules or other NH-pyrazole molecules are necessary to facilitate the transfer [45–49]; these auxiliaries must have centers able to establish hydrogen bonds, either HB acceptors, HB donors or both, like water. To test the reliability of our approach, we have calculated those of the parent pyrazole, as shown in Fig. 1 (all values in kJ mol<sup>−1</sup>). Similar structures for the unsubstituted pyrazole were published by Oziminski [49] who reported at the MP2/ B3LYP/6-311 + +G(d,p) level a barrier of  $\Delta E = 81.6$  kJ mol<sup>−1</sup> to compare with  $\Delta E = 82.2$  kJ mol<sup>−1</sup> of Fig. 1, right side. Note that an experimental study has demonstrated the role of water in the prototropy of phenylmethyl-pyrazole [50].

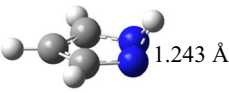
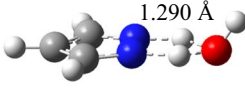
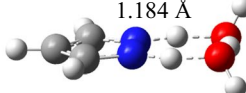
Then, we have carried out the same calculations on **1** obtaining very similar results, *i.e.*, according to the calculations in the gas phase the effect of the 4-trimethylsilyl is insignificant, as shown in Fig. 2. Experimentally, there is a noticeable decrease, from 61.9 to 49.8 kJ mol<sup>−1</sup> (12.1 kJ mol<sup>−1</sup>).

Continuum solvation effects, estimated with the PCM approximation [51], reduce the barrier slightly (Table 3), but it remains overestimated. Considering that the presence of two water molecules continues to be a model, the results are satisfactory. We have also calculated the value with

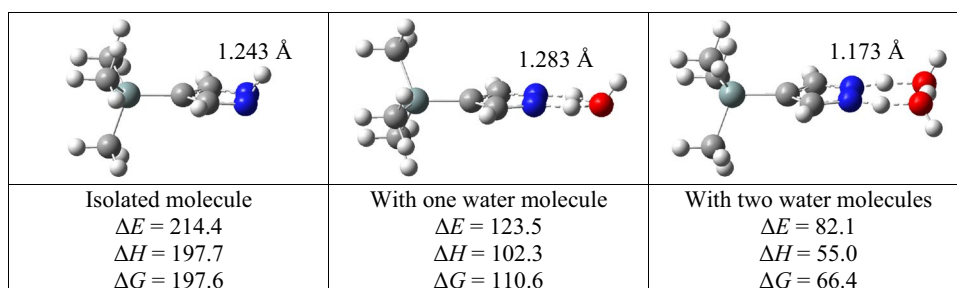
**Table 2** Dynamic processes present in pyrazole and in trimethylsilyl-1*H*-pyrazoles. Barriers in kJ mol<sup>−1</sup>; the calculated values at 298.15 K

Pyrazole	Solvent	Barrier	Ref	$\Delta G$ calc
Prototropy				
Unsubstituted pyrazole	DMSO	61.9	[43, 44]	68.7
4-Trimethylsilyl <b>1a/1b</b>	CD <sub>3</sub> OD	49.8	[5]	66.4
Silylotropy				
1-Trimethylsilyl <b>2a/2b</b>	Neat liquid	96.7	[29]	103.6
1-Trimethylsilyl-4-methyl <b>3a/3b</b>	Neat liquid	94.4 ± 1.0	[5, 22]	102.7

**Fig. 1** Transition states corresponding to the proton transfer of parent pyrazole. The N–H distances are indicated

		
Isolated molecule $\Delta E = 212.9$ $\Delta H = 196.3$ $\Delta G = 196.6$	With one water molecule $\Delta E = 122.6$ $\Delta H = 101.7$ $\Delta G = 112.2$	With two water molecules $\Delta E = 82.2$ $\Delta H = 54.6$ $\Delta G = 68.7$

**Fig. 2** Transition states corresponding to the proton transfer of 4-trimethylsilyl-1*H*-pyrazole (1). The N–H distances are indicated



**Table 3** Dynamic processes present in NH-pyrazoles. Calculated barriers in  $\text{kJ}\cdot\text{mol}^{-1}$  including two water or two methanol molecules and PCM effects

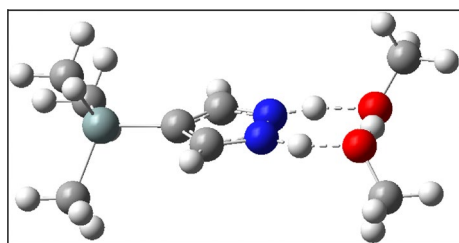
Pyrazole	Solvent	Barrier	Ref	+ PCM at 298.15 K	+ PCM at the $T_c^d$
Unsubstituted pyrazole	DMSO	61.9	[43, 44]	66.5 <sup>a</sup>	68.3
4-Trimethylsilyl <b>1a/1b</b>	CD <sub>3</sub> OD	49.8	[5]	64.2 <sup>b</sup>	61.6
4-Trimethylsilyl <b>1a/1b</b>	CD <sub>3</sub> OD	49.8	[5]	60.4 <sup>c</sup>	58.4

<sup>a</sup>PCM(DMSO) with two water molecules

<sup>b</sup>PCM(methanol) with two water molecules

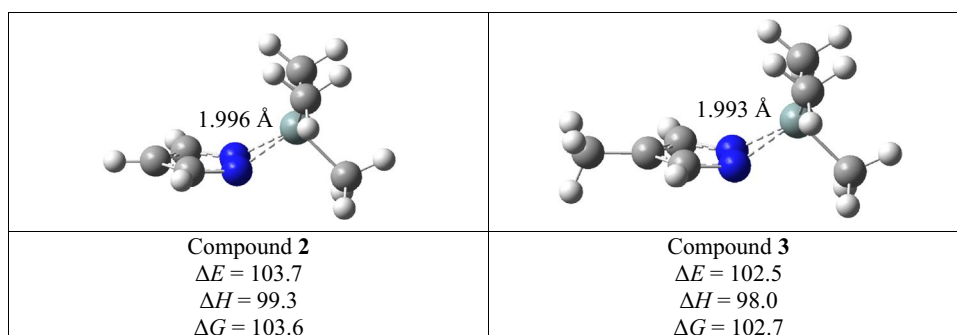
<sup>c</sup>PCM(methanol) with two methanol molecules

<sup>d</sup>temperature of coalescence for unsubstituted pyrazole, 337 K, for compound **1**, 229 K



**Fig. 3** Transition state of 4-trimethylsilyl-1*H*-pyrazole (1) with two methanol molecules. The N–H distances are indicated

**Fig. 4** Transition states corresponding to the TMS transfer of *N*-trimethylsilyl derivatives **2** and **3**. The N–Si distances are indicated



methanol instead of water and PCM/methanol (Fig. 3 and Table 3), obtaining a lower value.

The characteristic out-of-plane TSs of the silylotropy [4] (Fig. 4) are very similar for **2** and **3**. The calculated barriers show that the 4-methyl group produces almost no effect, and that of **3** is a slightly lower in agreement with the experimental values (Table 2), but overestimated, ratio calculated/experimental, 1.07 for **2** and 1.09 for **3**.

## 4 Conclusions

Whereas the agreement between calculated and experimental chemical shifts for the three derivatives, 4-trimethylsilyl-1*H*-pyrazole (**1**), 1-trimethylsilyl-1*H*-pyrazole (**2**) and 1-trimethylsilyl-4-methyl-1*H*-pyrazole (**3**), was expected due to our previous experience on these relationships, the part concerning the barriers to the dynamic processes (prototropy and silylotropy) is more complex. When the migrating group is the trimethylsilyl, the calculations do not involve any particular problem and the results are good. On the other hand, prototropy needs the assistance of solvent molecules that other authors [49, 52] and ourselves [45–48] have modeled with water molecules, which is only an acceptable simplification.

**Supplementary Information** The online version contains supplementary material available at <https://doi.org/10.1007/s00214-022-02936-z>.

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## Declarations

**Conflict of interest** The authors declare that they have no conflict of interest.

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