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Dynamic ^{1}H NMR study of 4-methylphenoxyimidoyl azides: conformational or configurational isomerisation?

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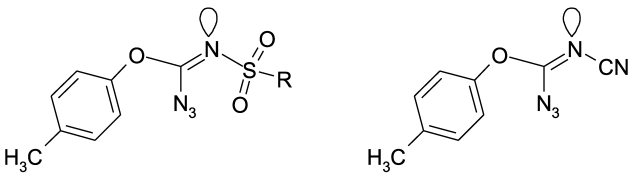
Abstract—Dynamic ^{1}H NMR (500 MHz) investigation of 4-methylphenoxyimidoyl azides (4-CH_3–C_6H_4–O–C═N–Y)–N_3, Y=4-CH_3–C_6H_4–SO_2–, 4-Br–C_6H_4–SO_2–, $C_6H_5SO_2$–, CH_3–SO_2–, –CN in acetone-d_6 at temperature range of 195–280 K is reported. The observed free energy barrier (almost 12 kcal mol^{-1}) is attributed to conformational isomerisation about the N–S bond for Y=4-CH_3–C_6H_4–SO_2–, 4-Br–C_6H_4–SO_2–, $C_6H_5SO_2$–, CH_3–SO_2– and (almost 14 kcal mol^{-1}) to configurational isomerisation (*E*/*Z*) about C═N bond for Y=–CN.

1. Introduction

Nitrogen-containing compounds are very important precursors to a wide range of biologically active molecules such as amino acids, antibiotics, alkaloids, imines and many others.[1–7] The two most important aspects of this class of compounds have been the stereo-regio-selectivity of their synthesis[1–7] and the energy barrier to nitrogen interconversion.[7–17] Both aspects have made very important contributions to the physical and/or chemical properties. Thus, the interconversion about nitrogen bonds of nitrogen-containing organic molecules has been a cornerstone of research interests for the last half century.[7–16]

Organoazides are one of the most important synthetic intermediates for the preparation of nitrogen-containing organic compounds. The azido functionality not only reacts with nucleophiles and electrophiles but also serves as a nitrene precursor for thermolysis or photolysis. In recent years, imidoyl azides have been used as a convenient reagent to generate nitrenes.[16–22] Recently, we reported a dynamic ^{1}H NMR study of 2-(*tert*-butoxymethyl)-1-[*N*′-(4-methylbenzenesulfonyl) (4-methylphenoxy) imidoyl] aziridine **8** (Scheme 4).[17]

We wish to describe herein the dynamic NMR studies of imidoyl azides **1**–**5** and factors that influence the interconversion energy barrier of the isomers (Scheme 1).



1 : R = 4-$CH_3C_6H_4$
2 : R = C_6H_5
3 : R = 4-BrC_6H_4
4 : R = CH_3

5

Scheme 1.

The question raised here, is whether the free energies observed correspond to conformational isomerisation (rotation) about the N–S bond or configurational isomerisation (*E*/*Z*) about the C═N bond?

2. Results and discussion

The imidoyl azides **1**–**5** were prepared from 5-(4-methylphenoxy) tetrazole **6** and electron-withdrawing reagents such as TsCl, $PhSO_2Cl$, BsCl, MsCl, and Br–CN, respectively, using a previously described method,[18] (Scheme 2).

The results of the temperature dependence study of the ^{1}H NMR (500 MHz) spectra of imidoyl azides **1**–**5** are shown in Table 1. Gradual cooling of the samples broadens the ^{1}H NMR signals of azides **1**–**5**, which coalesce and then, at lower temperatures split into two set of signals. For example, variable temperature ^{1}H NMR (500 MHz) spectra

Keywords: Dynamic ^{1}H NMR; Imidoyl azides; Tetrazoles; *E*/*Z* isomerisation; Rotation about the N–S bond.
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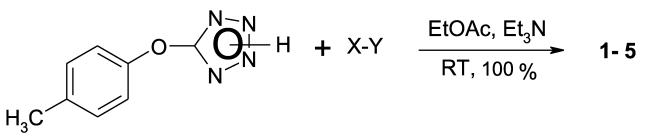


6

Y = 4-$CH_3C_6H_4SO_2$, $C_6H_5SO_2$, 4-$BrC_6H_4SO_2$, CH_3SO_2, CN

X = Cl, Br

Scheme 2.

and the expanded peaks corresponding to the methyl groups in the 2.0–2.5 ppm region (2.400, 2.363, 2.283 and 2.260) have showed for imidoylazide **1** at the lowest temperature reached (195 K) in Figures 1 and 2, respectively. A mixture of two diastereomers with almost equal populations is displayed at low temperatures. The peaks corresponding to the methyl group of 4-methylphenoxy groups were utilized in our calculations.

The rate constants, k, for the interconversion of the imidoyl azides **1**–**5** at the coalescence temperature (T_c) were calculated from Gutowsky–Holm equation ($k_c=\pi\Delta\nu/2^{-1/2}$). Assuming the transmission coefficient, κ, to be unity the free energy of activation ($\Delta G^{\ddagger}$), was calculated from Eyring equation ($\Delta G^{\ddagger}=RT_c[\ln T_c-\ln k_c+23.76]$).[12–14,17] The Gutowsky–Holm equation is strictly valid for two states having equal populations, but the errors introduced by these deviations are small.[13,14,17] The imidoyl azides **1**–**4**, all showed similar energies of activation (see Table 1) with small variations in peak height for the two isomers. However, the free energy of activation for compound **5** is higher by about 2 kcal mol^{-1}.

The energy barrier for **5** (14.2 kcal mol^{-1}) corresponds to configurational isomerisation (*E*/*Z*) which is the interconversion of nitrogen about the C=N bonds. Similar results are reported for *N*-cyano-*O*-phenylisoureas **7** [14.4 kcal mol^{-1}, T_c=6 °C (279 K)] by Garratt and co-workers[13] and related compounds have energy barriers higher than 15 kcal mol^{-1}[13] (Scheme 3). Other examples of nitrogen interconversion (*E*/*Z* isomerisation) of

Table 1. Dynamic ^{1}H NMR data for imidoyl azides **1**–**5** in acetone-d_6

Compound	δ (ppm)	Isomers ratio	The lowest temperature reached (K)	$\Delta\nu$ (Hz)	T_c, °C (K)	k (s^{-1})	$\Delta G^{\ddagger}$ (kcal mol^{-1})
1	2.283, 2.260[a]	1.0:2.0	195	11.50	−41 (232)	26	12.4
1	2.400, 2.363[b]	—	—	18.50	−30 (243)	41	12.7
2	2.292, 2.279[a]	1.0:1.3	223	6.50	−38 (235)	14	12.4
3	2.288, 2.269[a]	1.0:1.2	213	9.50	−38 (235)	21	12.2
4	2.304, 2.289[a]	1.0:2.1	203	7.50	−38 (235)	17	12.3
4	3.181, 2.945[c]	—	—	118.03	−25 (258)	262	12.2
5	2.341, 2.298[a]	2.0:1.0	233	21.51	+8 (280)	48	14.2

[a] The chemical shift corresponding to protons of methyl of 4-methylphenoxy group.
[b] The chemical shift corresponding to protons of methyl of Ts group.
[c] The chemical shift corresponding to protons of methyl of Ms group.

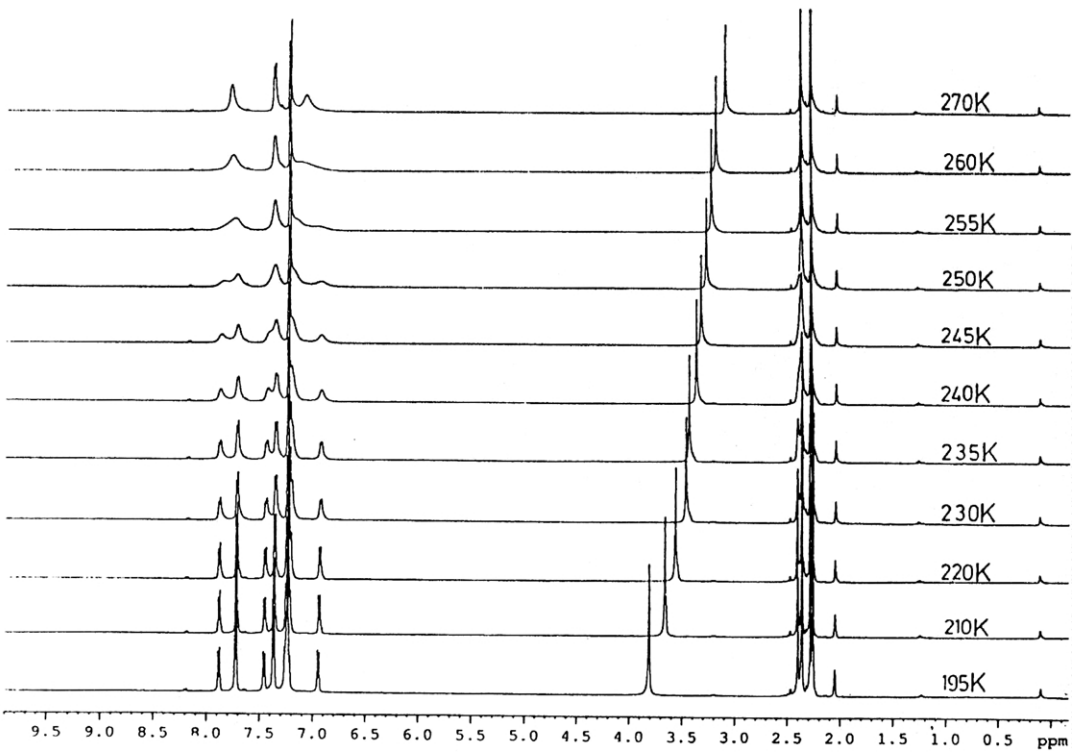


Figure 1. Variable temperature ^{1}H NMR (500 MHz) spectra for imidoylazide **1**.

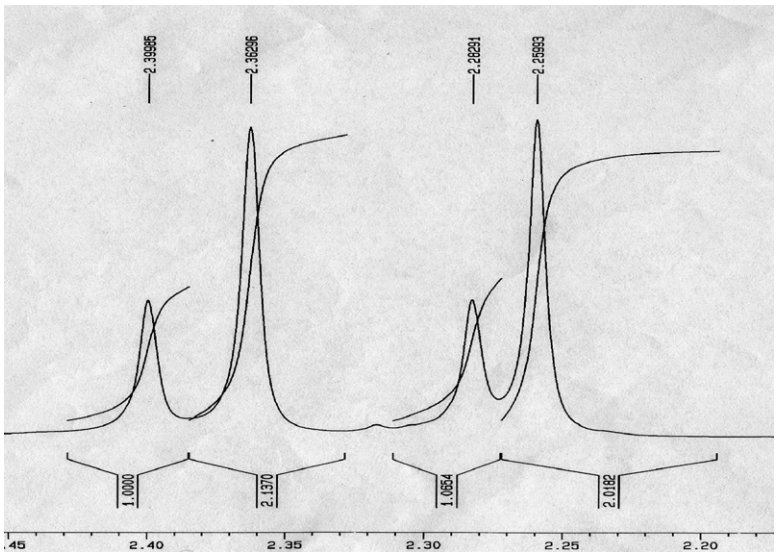
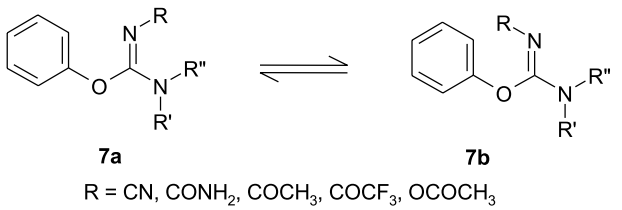


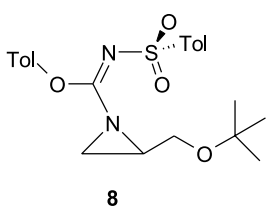
Figure 2. ^{1}H NMR (500 MHz) the expanded spectrum of methyl groups in the 2.0–2.5 ppm region (2.400, 2.363, 2.283 and 2.260) for imidoylazide **1** in CD_3CO at 195 K.



Scheme 3.

N-substituted imines are reported to have energy barriers higher than 15 kcal mol^{-1}.[12–17]

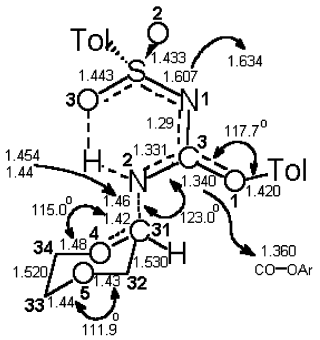
We also found a very high energy barrier (more than 24 kcal mol^{-1}) for the interconversion of nitrogen about the C=N bond in 2-(*tert*-butoxymethyl)-1-[*N*′-(4-methylbenzenesulfonyl)(4-methylphenoxy) imidoyl] aziridine **8** (Scheme 4).[16,17] Above 403 K, in nitrobenzene, there is competition between the imine interconversion and the aziridine rearrangement.[16,17] The detailed investigations of the imine interconversion and the characterization of the new compound **1X** are now underway.



Scheme 4.

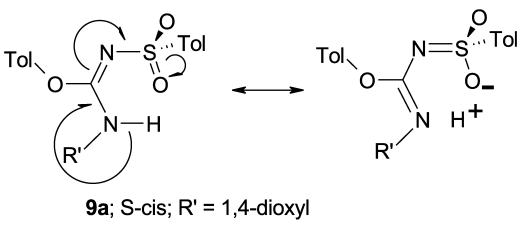
Azides **1**–**4** show an energy barrier which is lower by nearly 2 kcal mol^{-1}. These barriers represent the lower energy conformational isomerisation about the N–S bond (Table 1).

Recently, we reported X-ray conformational and configurational analysis of *N*-2-(1,4-dioxane)-*N*′-(*p*-methylbenzenesulfonyl)-*O*-(*p*-methylphenoxy) isourea **9** (Scheme 5).[19] The X-ray crystallographic analysis showed that the S=O3



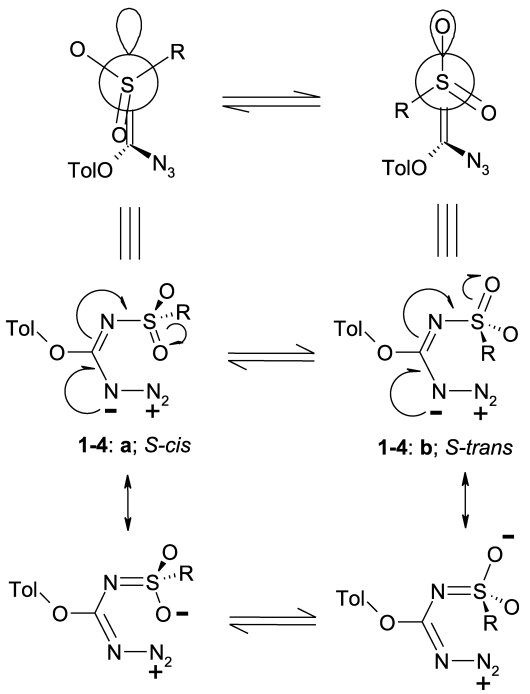
Scheme 5.

bond retains *s-cis* conformation with the C3=N1 bond (the torsion angle is almost equal to zero). In addition, there is a relatively strong intramolecular hydrogen bond between the N–H and the oxygen of S=O3 (Scheme 5). The *s-cis* conformation of S=O3, C3=N1 bonds and the S=O3···H–N hydrogen bonding helps the formation of a stable six-membered ring. This indicates the S=N1 bond has double bond character. This double bond character may be a result of hyperconjugation (Scheme 6).



Scheme 6.

The imidoyl azides **1**–**4** should form similar conformations (Scheme 7). The two main conformers, *s-cis* and *s-trans*, are the favored geometries. The *s-cis* in compounds **9** and **1**–**4** should be more stable than *s-trans*, because, the negative

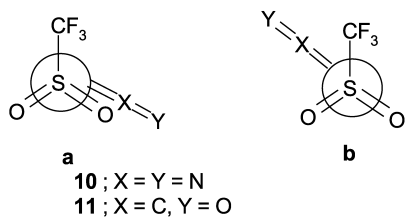


Scheme 7.

charge density on oxygen atom of S═O bond is neutralized by the positive charge on the hydrogen and nitrogen atoms, respectively.

However, the stability of the *s-cis* form of compound **9** is much more than imidoyl azides **1**–**4**. In the former case, the intramolecular hydrogen bond is stronger than electrostatic attraction. In other words, the energy barrier for the rotation about the N–S bond in **9** is much higher than that of imidoyl azides **1**–**4**.[16] Other similar examples have previously been conclusively demonstrated for diazoketones.[23,24] The diazoketones exist as an equilibrium mixture of *s-cis* and *s-trans* conformations, see the resonance structure in Scheme 7.

Haist and co-workers recently studied the structure and conformational properties of trifluoromethanesulfonyl azide **10** ($F_3CSO_2N_3$) and trifluoromethanesulfonyl isocyanate **11** (F_3CSO_2NCO) by electron diffraction and theoretical methods.[25] They concluded that both compounds posses a single conformation with eclipsed (*s-cis*) or nearly eclipsed orientation of the NCO or N_3 group relative to one S═O double bond (Scheme 8). Furthermore, they reported a rotation energy barrier of 10.3 kcal mol^{-1} about the N–S bond for compound **10**. The same orientation has been also observed for FSO_2NCO and $ClSO_2NCO$.[25]



Scheme 8.

Indeed, there are several investigations on the energy barriers of the rotation about the N–S bond (in sulfenamides and sulfinamides) indicating energies greater than 12 kcal mol^{-1}.[26–32]

3. Conclusion

The imidoyl azides **1**–**4** show quite similar energies of activation indicating that the substitute R has no influence on the observed energy barrier, while the nature of the substituent attached to the imine nitrogen has a significant effect on the energy barrier of *E*/*Z* isomerisation.[12–17] The proton chemical shifts of the R group are affected more than the protons of methyl or phenyl of the phenoxy group (see compounds **1** and **4** in Table 1, Figs. 1 and 2 and Scheme 1). Both effects are induced by rotation about the N–S bond. We attribute the observed dynamic ^{1}H NMR effect for **1**–**4** to rotation about the N–S bond.

4. Experimental

4.1. General

^{1}H NMR spectra were recorded by BRUKER AVANCE DRX500 (500 MHz) and Varian EM 390 (90 MHz). The IR spectra were obtained on a SHIMADZU-470 and SHIMADZU ZU-435. Mass spectra were analyzed by Finnigan-Matt 8430 instruments (70 eV). Elemental analysis was performed using Heraeus CHN-O-Rapid analyser. Melting points were taken by the Electrothermal 9100 and the GallenKamp melting point apparatus and were uncorrected.

Variable temperature ^{1}H NMR spectra were obtained on BRUKER AVANCE DRX500 (500 MHz) and calibrated with a standard methanol sample.[33] The temperature was measured at the probe (±0.1 °C). Samples were allowed to equilibrate for 10 min at each temperature before recording the spectrum.

4.2. Chemicals

All starting materials and solvents were purified with appropriate purification techniques before use.[34] Tetrazoles were prepared according to literature.[16–22]

4.3. The general procedure for preparation of the imidoyl azides 1–5

Method A.[16–22] To a solution of tetrazole **6** (10 mmol) in 30 mL of peroxide-free anhydrous THF was added **X**–**Y** (10 mmol) in 10 mL THF, with cooling in an ice-salt bath under nitrogen (or argon). Triethylamine (10 mmol) in 10 mL THF was added over a period of 30 min. The mixture was stirred and allowed to come to room temperature, over several hours. Filtration, washing with THF, evaporation of the THF solutions, and chromatography on silica gel, gives imidoyl azides. All imidoyl azides recrystallize from chloroform (or dichloromethane) and petroleum ether (40–60 °C).

Method B.[18] To a stirred solution of tetrazole **6** (10 mmol) and **X**–**Y** (10 mmol) in 20 mL ethyl acetate, in a 50 mL flask equipped with a stopper, triethylamine (13 mmol) was added dropwise over 5 min at room temperature. The mixture was stirred over 2–5 h. Reaction progress was monitored by TLC. The filtrate was washed with ethyl acetate. Evaporation of the ethyl acetate solution (under vacuum and at room temperature), gave pure imidoyl azides in a quantitative yield. All imidoyl azides recrystallize from chloroform (or dichloromethane) and petroleum ether (40–60 °C).

N′-(4-Methylbenzenesulfonyl) (4-methylphenoxy) imidoyl azide **1**, *N*′-(benzenesulfonyl) (4-methylphenoxy) imidoyl azide **2** and *N*′-(cyano) (4-methylphenoxy) imidoyl azide **5** were prepared using the methods described above, as reported earlier[18] (Scheme 2).

4.3.1. *N*′-(4-Bromobenzenesulfonyl) (4-methylphenoxy) imidoyl azide 3. According to the general procedure (Method B) using 5-(4-methylphenoxy) tetrazole **6** and BsCl afforded white crystals which soften on handling; [found: C, 43.61; H, 2.63; N, 13.89. $C_{14}H_{11}BrN_4O_3S$ requires C, 42.54; H, 2.81; N, 14.18%]; IR (KBr); 3060 (w), 2900 (w), 2720 (w), 2650 (w), 2170 (w), 2110 (w), 1610–1560 (vs), 1490 (s), 1330 (s), 1270 (s), 1180 (s), 1140 (s), 1070 (m), 1000 (m), 810 (s), 750 (s), 620 (s), 590 (s), 540 (s) cm^{-1}. ^1H NMR (500 MHz, $CDCl_3$, 300 K), δ ppm; 2.37 (s, 3H, CH_3–C_6H_4–O), 7.09 (d, J=8.2 Hz, 2H, CH_3–C_6H_4–O), 7.24 (d, J=8.2 Hz, 2H, CH_3–C_6H_4–O), 7.77 (d, J=8.5 Hz, 2H, Br–C_6H_4–SO_2), 7.83 (d, J=8.5 Hz, 2H, Br–C_6H_4–SO_2). Mass spectrum: *m*/*z* (%)=396 [2, M+2 (^{81}Br)], 394 [2, M (^{79}Br)], 326 (15, $^{81}BrC_6H_4NTol$ from Chapman rearrangement[17]), 324 (15, $^{79}BrC_6H_4NTol$ from Chapman rearrangement[17]), 221 (47, $^{81}BrC_6H_4SO_2$), 219 (47, $^{79}BrC_6H_4SO_2$), 157 (50, $^{81}BrC_6H_4$), 155 (50, $^{79}BrC_6H_4$), 119 (20, Tol-N_2), 107 (100, TolO), 91 (50, Tol).

4.3.2. *N*′-(Methylsulfonyl) (4-methylphenoxy) imidoyl azide 4. According to the general procedure (Method B) using 5-(4-methylphenoxy) tetrazole **6** and MsCl afforded a white crystals, mp 88–90 °C; [found: C, 42.70; H, 4.11; N, 21.46. $C_9H_{10}N_4O_3S$ requires C, 42.51; H, 3.96; N, 22.04%]; IR (KBr); 3000 (w), 2800 (w), 2700 (w), 2175 (s), 2120 (s), 1620–1560 (vs), 1485 (s), 1310 (vs), 1195 (s), 1140 (vs), 1040 (s), 1000 (s), 820 (s), 770 (s), 600 (s), 530 (s) cm^{-1}. ^1H NMR (500 MHz, $CDCl_3$, 300 K), δ ppm; 2.35 (s, 3H, CH_3–C_6H_4–O), 3.01 (s, 3H, CH_3–SO_2), 7.20 (d, J=8.5 Hz, 2H, CH_3–C_6H_4–O), 7.27 (d, J=8.5 Hz, 2H, CH_3–C_6H_4–O). Mass spectrum: *m*/*z* (%)=254 (1, M), 184 (5, $TolNSO_2$ from Chapman rearrangement[17]), 175 (20, $TolOCN_4$), 119 (9, Tol-N_2), 108 (27, TolOH), 91 (100, Tol), 79 (10, CH_3SO_2).

Acknowledgements

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