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Synthesis, structure, and isomerism of *N*-2,4-dinitrophenylbenzotriazoles

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Dedicated to Professor Guy Ourisson in memoriam

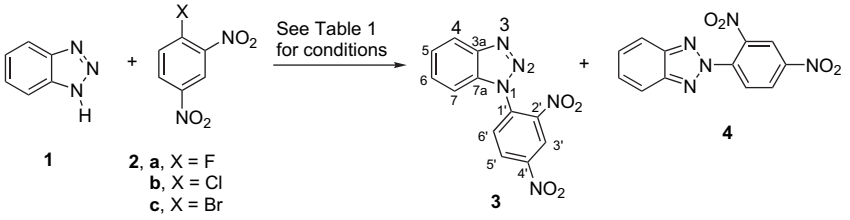
Abstract—Both isomers of *N*-(2′,4′-dinitrophenyl)benzotriazole, the 1(3)- and the 2-substituted, have been characterized and their reciprocal isomerism was studied. Cross-experiments in the presence of 5(6)-nitro-1*H*-benzotriazole proved that the isomerization of 2-(2′,4′-dinitrophenyl)-2*H*-benzotriazole into the 1-isomer occurs by an intermolecular mechanism. The reported reaction of 5(6)-nitro-1*H*-benzotriazole with 1-chloro-2,4-dinitrobenzene has been reexamined discovering that there is an error in the proportions of *N*-substituted isomers. A possible explanation for the observed isomerizations was proposed. Identification of all compounds by multinuclear magnetic resonance, including solid-state studies, has been achieved.

1. Introduction

In 1966–1967 three groups studied simultaneously the reaction between 1*H*-benzotriazole (**1**) and 1-halo-2,4-dinitrobenzenes (**2**) (Scheme 1).[1–3] Some of us carried out the reaction of **2a** and **1** in xylene at reflux and obtained exclusively the 1-isomer **3**.[2] On the other hand, Kamel et al. carried out the reaction of **2b** and **1** in ethanol in the presence of sodium acetate obtaining both isomers **3** and **4** in a 70:30 ratio.[3] Wilshire[1] also did the reaction of **2a** and **1** in a variety of solvents and reported that the ratio of **3/4** is 98:2 in benzene and 74:26 in ethanol, the highest proportion of **4** being obtained in DMF (62:38 ratio). The 1-isomer **3** has long been known since Borsche and Rantscheff prepared it (mp 186–187 °C) by cyclization of the mono-(2′,4′-dinitrophenyl)-*o*-phenylenediamine with nitrous acid.[4,5] Afterward, compounds **3** and **4** have been published several times,[6–12] but only Davydov et al.[8] have described again the formation of both isomers, 1-(2′,4′-dinitrophenyl)-1*H*-benzotriazole (**3**) and 2-(2′,4′-dinitrophenyl)-2*H*-benzotriazole (**4**).

We have summarized in Table 1 all the results reported so far on these two compounds.

In view of the inconsistency in the melting points reported in Ref. 8 and, especially, the result that a reaction of N-arylation is so dependent of the experimental conditions varying from pure **3** to pure **4** (even assuming that minute quantities



Scheme 1. Formation of dinitrophenylbenzotriazoles (**3** is represented in the *Z* conformation with the nitro group pointing toward the N2 of the benzotriazole). We have extended the *E*/*Z* nomenclature to the conjugate N1-aryl single bond.

Keywords: Benzotriazoles; 2,4-Dinitrophenyl group migration; Kinetics; NMR; GIAO/B3LYP/6-31G* absolute shieldings; B3LYP/6-31G** stabilization energies.
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Table 1. Literature results on benzotriazole derivatives **3** and **4**

Entry	**2**, X	Conditions	Isomer 1-R **3**	Isomer 2-R **4**	Ref.	**3/4** ratio	NMR
1	**a**, F	Diff. solv., rt	185–187 °C	167–168 °C	1	98:2[a] 74:26[b]	^{1}H
2	**a**, F	Xylene, reflux	182–183 °C	—	2	>99	^{1}H
3	**b**, Cl	EtOH, reflux	186 °C	165 °C	3,12	70:30	None
4	**b**, Cl	Toluene, reflux	182–184 °C	—	6,12	>99	^{1}H
5	**c**, Br	DMSO/NaH/rt	—	166–167 °C[c]	7	<0.01	^{1}H, ^{13}C
6	**b**, Cl	PTC	232 °C	192 °C	8	76:19[d]	^{1}H
7	**a**, F	Cs_2CO_3, DMF, rt	185 °C	—	9	>99	None
8	**b**, Cl	PTC; MW	181–182 °C	—	10	>99	^{1}H
9	**b**, Cl	Ionic liquid	Not reported	—	11	>99	None
10	This work		185.7 °C (DSC)	167.9 °C (DSC)	—	62:38[e]	^{1}H, ^{13}C, ^{15}N

[a] In benzene.
[b] In ethanol.
[c] The authors do not assign the structure but from the melting point and the ^{1}H and ^{13}C NMR data they report that the compound is undoubtedly the 2-isomer **4**.
[d] For 12 h with K_3PO_4.
[e] In DMF.

of the other isomer were lost in the purification), we decided to repeat the synthesis (Table 1, entry 10) and to carry out a complete NMR study as well as to examine the relative stabilities of compounds **3** and **4**.

2. Results and discussion

2.1. Synthesis and DSC melting points

We have used the Wilshire's procedure to obtain both isomers of *N*-(2′,4′-dinitrophenyl)benzotriazole, the 1(3)- and the 2-substituted, using DMF as solvent.[1] The melting points were determined by DSC as being very close to those reported by all authors save those of Beletskaya et al.,[8] which should be considered erroneous. We have also noted, during the DSC experiments, the absence of any phase transition.

2.2. NMR characterization

Although there are some previous reports on the NMR spectra of 1-(2′,4′-dinitrophenyl)-1*H*-benzotriazole (**3**) and 2-(2′,4′-dinitrophenyl)-2*H*-benzotriazole (**4**) (see Table 1), we have recorded the ^{1}H (Table 2), ^{13}C (Table 3), and ^{15}N NMR spectra (Table 4) in DMSO-d_6 solution and for the two last nuclei also in the solid state (CPMAS).

A NOESY experiment in DMSO-d_6 solution of compound **3** shows a correlation between H6′ and H7 (Fig. 1), which is consistent with a *Z* conformation in such polar solvent, contrary to the theoretical predictions in the gas phase (see Section 2.3).

The assignments were based on the usual 2D methodologies and are consistent with literature results on benzotriazoles

Table 2. ^{1}H NMR (δ in ppm and *J* in Hz) of **3** and **4** in DMSO-d_6

Compound	H-4	H-5	H-6	H-7	Others
3	8.27 (ddd), $^{3}J_{H5}$=8.6, $^{4}J_{H6}$=$^{5}J_{H7}$=0.9	7.60 (ddd), $^{3}J_{H6}$=7.7, $^{4}J_{H7}$=0.9	7.75 (ddd), $^{3}J_{H7}$=8.3	7.85 (ddd)	9.07 (d, 1H, H-3′, $^{4}J_{H\text{-}5'}$=2.5); 8.80 (dd, 1H, H-5′, $^{3}J_{H\text{-}6'}$=8.8); 8.39 (d, 1H, H-6′)
4	8.04 (m), $^{3}J_{H5}$=8.8, $^{5}J_{H7}$=0.8	7.58 (m), $^{3}J_{H6}$=6.6, $^{4}J_{H7}$=0.9	7.58 (m)	8.04 (m)	9.02 (d, 1H, H-3′, $^{4}J_{H\text{-}5'}$=2.5); 8.72 (dd, 1H, H-5′, $^{3}J_{H\text{-}6'}$=8.9); 8.51 (d, 1H, H-6′)

Table 3. ^{13}C NMR (δ in ppm and *J* in Hz) of **3** and **4** in DMSO-d_6 and in the solid state

Compound	C-4	C-5	C-6	C-7	C-3a	C-7a
3 (DMSO-d_6)	120.1, ^{1}J=166.9, ^{3}J=7.6	125.6, ^{1}J=163.9, ^{3}J=7.5	129.8, ^{1}J=164.3, ^{3}J=7.9	110.3, ^{1}J=170.0, ^{3}J=8.3	145.3, ^{2}J=10.0, ^{3}J=4.9	132.4, ^{3}J=10.6, ^{3}J=6.5
3 (CPMAS)[a]	119	127	130	111	146	134
4 (DMSO-d_6)	118.4, ^{1}J=168.1	129.2, ^{1}J=163.2, ^{3}J=8.2, ^{2}J=1.6	129.2	118.4	145.2, ^{3}J=9.4, ^{3}J=5.4	145.2
4 (CPMAS)	121.4[b]	122.9[b]	124.6[b]	115.1[b]	145.4[b]	140.7[b]
Other signals						
3 (DMSO-d_6)	147.4 (C-4′, ^{3}J=10.6, ^{2}J=5.1); 144.1 (C-2′, ^{3}J=8.2, ^{2}J=4.9); 132.6 (C-1′, ^{3}J=9.8, ^{3}J=6.9); 129.2 (C-5′); 128.9 (C-6′, ^{1}J=174.5); 121.8 (C-3′, ^{1}J=177.2, ^{3}J=5.1)					
3 (CPMAS)[a]	146 (C-4′); 146 (C-2′); 134 (C-1′); 130 (C-5′, C-6′); 124 (C-3′)					
4 (DMSO-d_6)	147.3 (C-4′, ^{3}J=10.6, ^{2}J=4.9, ^{2}J=3.3); 143.0 (C-2′, ^{3}J=7.9, ^{2}J=4.3, ^{4}J=1.6); 135.0 (C-1′, ^{3}J=9.8, ^{3}J=6.9, ^{2}J=2.0); 128.3 (C-5′, ^{1}J=176.2); 127.5 (C-6′, ^{1}J=176.3); 121.2 (C-3′, ^{1}J=177.1, ^{3}J=5.7, ^{4}J=1.6)					
4 (CPMAS)	146.2 (C-4′); 144.2 (C-2′); 131.5 (C-1′); 130.2 (C-5′); 129.1 (C-6′); 122.9 (C-3′)					

[a] Very broad signals, between 1.1 and 1.8 ppm of width.
[b] The assignment of these signals can be exchanged.

Table 4. ^{15}N NMR (δ in ppm) of compounds **3** and **4** in DMSO-d_6 and in the solid state

Compound	N-1	N-2	N-3	Other	
3 (DMSO-d_6)	−156.9	−4.1	−29.7	−15.1 (NO_2-2′)	−15.8 (NO_2-4′)
3 (CPMAS)	n.o.	n.o.	n.o.	n.o.	n.o.
4 (DMSO-d_6)	−62.8	−123.0	−62.8	−14.5 (NO_2-2′)	−16.1 (NO_2-4′)
4 (CPMAS)	−71.9	−122.8	n.o.	−12.4 (NO_2-2′)	−15.8 (NO_2-4′)

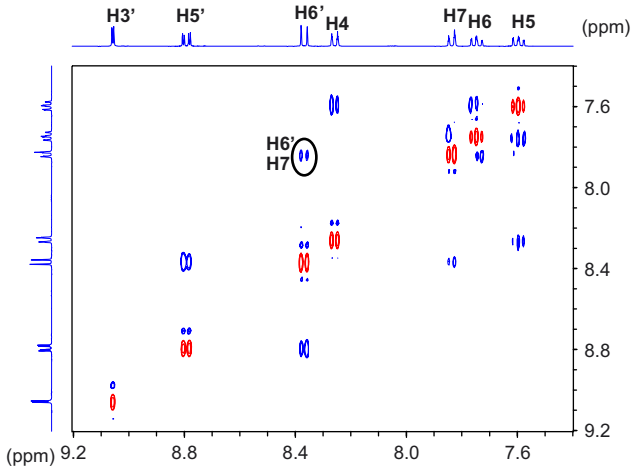


Figure 1. NOESY spectrum of compound **3** in DMSO-d_6.

and other related azole derivatives.[1,7,13–16] It should be noted that in solution both isomers are easily identified on simple symmetry considerations. For instance, the benzotriazole moiety in the ^{1}H NMR of isomer **3** appears as an ABCD system while in isomer **4** the system is an AA′BB′ (see Table 2). This is due to the free rotation (or, at least, liberation) about the N−C inter-ring bond. This freedom disappears in the solid state (Table 3). Since the broadening of the ^{13}C signals of compound **3** is unspecific, it is probably due to the planar structure of the compound.[17,18] Note for compound **4** in the solid state the splitting of the signals of the benzotriazole ring. Its structure is presumably planar with a stabilizing orthogonal interaction[19–21] between the N-atom of the nitro group and the N-3 atom (Fig. 2). This makes all the atoms of the 2*H*-benzotriazole ring different, but it cannot be excluded, as an alternative explanation, the presence of two independent molecules in the unit cell.

The ^{15}N NMR results (Table 4) are less useful because in several cases some signals could not be detected. This is particularly true for isomer **3** where no signal was observed in the CPMAS spectrum.

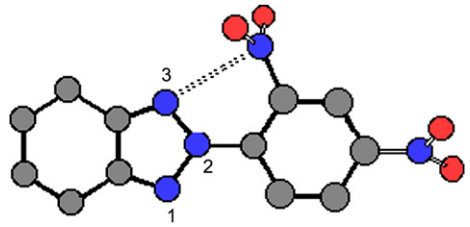


Figure 2. View of compound **4** showing the asymmetry generated by the *ortho*-nitro group.

In the case of compound **4** in the solid state, only the signal of N-3 was not observed. To estimate its position, GIAO/B3LYP/6-31G* calculations were carried out on this compound. Since there is a very good correlation between experimental chemical shifts and calculated absolute shieldings, the missing nitrogen signal should appear at about −60 ppm (Table 5).

2.3. Theoretical calculations

We have carried out density functional theory calculations (B3LYP/6-31G**) on compounds **3** and **4** to know their relative stabilities. The results are reported in Table 6.

The most stable conformation of **3** in the gas phase has the nitro group pointed toward the benzene ring, **3***E*. Probably there is a C7−H···O=N hydrogen bond (calculated H···O distance is 2.86 Å). Isomer **4** has a N3···NO_2 distance of 2.90 Å (see Fig. 1) and a calculated geometry, which is rather similar to that of XEWLOA with a distance of 2.65 Å.

An important consequence drawn from the analysis of Table 6 values is that, although **3***E* is more stable than **3***Z* and **4**, the differences are small. Since the dipole moments of **3***Z* and **4** are larger than that of **3***E*, it is expected that an extra stabilization would occur in polar solvents.

2.4. Isomerization processes

First, we will report the most significant experiments carried out with compounds **3** and **4** in solution using ^{1}H NMR at 400 MHz to monitor the isomerizations. The spectra reported in Figure 3 correspond to the evolution of **4** in DMF-d_7 at 323 K.

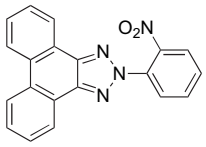
(1) Isomer **3** is indefinitely stable (experimentally 43 days) in DMSO-d_6 solution at 295 K in what concerns isomerization.
(2) Isomer **4** is indefinitely stable in chloroform solution.

Table 5. ^{15}N NMR, absolute shieldings (σ, in ppm) and experimental chemical shifts (δ in ppm) of compound **4**

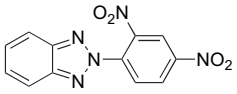
Atom	σ	δ	
		Experimental	Fitted[a]
N-1	−53.875	−71.91	−70.5
N-2	−3.483	−122.77	−123.7
N-3	−63.199	—	*−60.7*
NO_2-2′	−111.348	−12.39	−10.0
NO_2-4′	−105.9296	−15.88	−15.6
$MeNO_2$[b]	−117.75	00.00	

Predicted value is given in italics.
[a] $[\delta(^{15}N)=-(127.4\pm2.3)-(1.06\pm0.03)\sigma(^{15}N)$, $n=5$, $r^2=0.998]$.
[b] From Ref. 22.

Table 6. B3LYP/6-31G** energies (hartree), relative energies (kJ mol^{-1}), and other properties of compounds **3**, **4**, and XEWLOA



XEWLOA



4

Compound	**3***Z*	**3***E*	**4**	XEWLOA[a]
Energy	−1035.91225	−1035.913498	−1035.91351	—
E+ZPE	−1035.72124	−1035.72230	−1035.72185	—
E_{rel} (ZPE)	2.79	*0.00*	1.18	—
μ (Debye)	6.48	3.69	5.35	—
N2(1)−N1(2)−C1′−C2′ (°)	48.9	142.4	148.5	150.5
O−N−C2′−C1′ (°)	35.9	34.5	42.6	61.7
N2 (or N3)···NO_2 (Å)	3.02	4.20	2.90	2.65

[a] From CSD.[23]

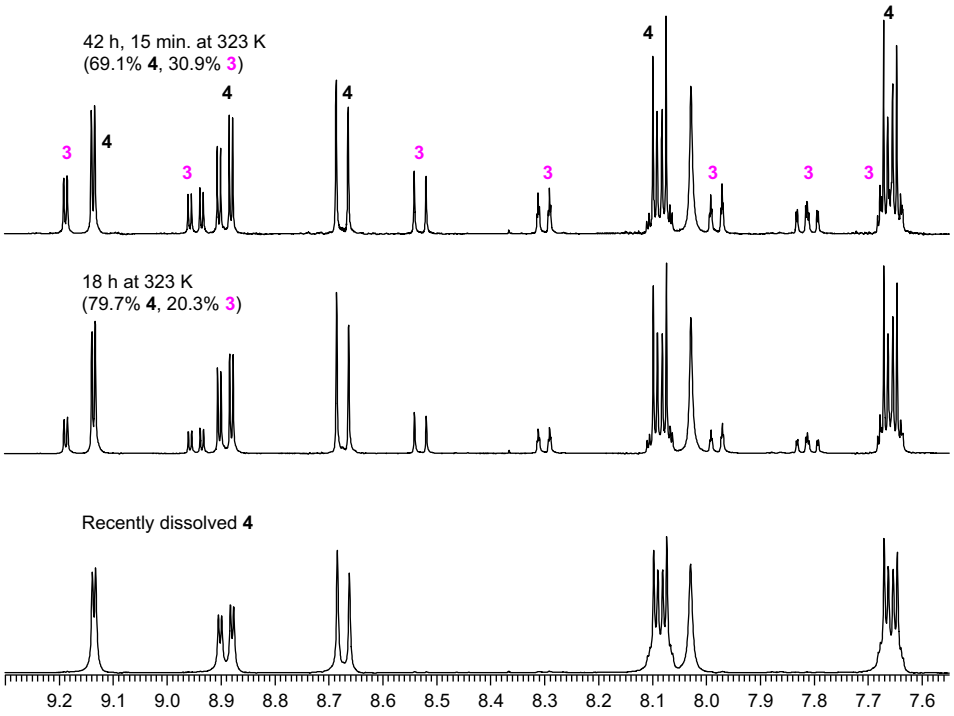


Figure 3. ^{1}H NMR spectra showing the isomerization in DMF-d_7 at 323 K of 2-isomer **4** into 1-isomer **3**.

(3) Isomer **4** in DMSO-d_6 solution slowly evolves to attain asymptotically a mixture of **3**+**4** in a ratio that slightly depends on the temperature, about 20% of **3** at 295 K and about 15% of **3** at 323 K. The rates of these two experiments are practically the same.
(4) Isomer **4** in DMF-d_7 solution slowly (but faster than in DMSO-d_6) evolves to attain asymptotically a 50:50 mixture of **3**+**4**.

The analysis of the kinetic data (see Supplementary data for Tables of data) is rather complex since there is no standard integrated equation that goes through all the points (see Section 4). We have assumed that the reaction proceeds to a state of equilibrium, which differs appreciably from completion. For the case when the forward and reverse reactions are of the first order, the integrated equation has the form $\ln[x_e/(x_e-x)]=(a_0k/x_e)t_{sec}$, where x_e is the concentration at the equilibrium and a_0 is the initial concentration, in our case of **4**.[24] Due to the fact that either the reaction is not an opposing reaction or that the forward and reverse reactions are not of the first order, in all our cases there is an intercept a_1 that cannot be assumed to be 0 because it is highly significant, $\ln[x_e/(x_e-x)]=a_1+(a_0k/x_e)t_{sec}$. We have explored other models and one of the best, which takes account of the curvature, is the use of $\sqrt{t_{sec}}$.

Applying the Eyring equation, we have obtained the following results (Eqs. 1–3):

$$\begin{aligned}\text{DMSO-}d_6,\ 295\ \text{K}&: a_1=(1.22\pm0.11),\\ \text{slope}&: (3.63\pm0.25)\times10^{-7},\\ k&=(7.56\pm0.52)\times10^{-8}\ \text{s}^{-1},\\ \Delta G^{\ddagger}_{295}&=(112.3\pm0.2)\ \text{kJ mol}^{-1}\end{aligned}\qquad(1)$$

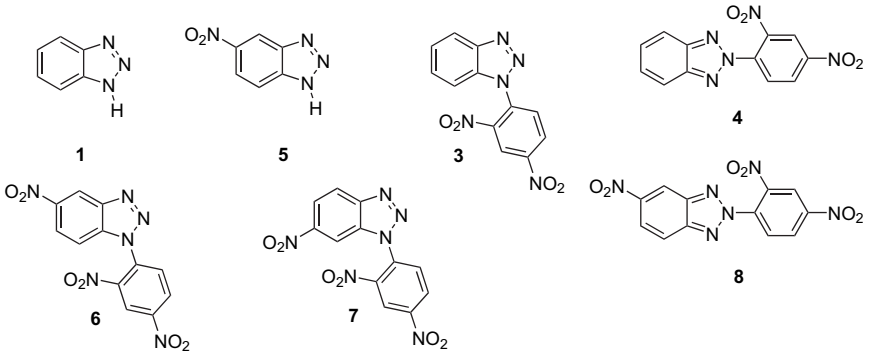
DMSO-d_6, 323 K: $a_1 = (1.14 \pm 0.07)$,
slope: $(5.16 \pm 0.25) \times 10^{-7}$,
$k = (8.17 \pm 0.40) \times 10^{-8}$ s^{-1},
$\Delta G^{\ddagger}_{323} = (123.0 \pm 0.1)$ kJ mol^{-1} (2)

DMF-d_7, 323 K: $a_1 = (0.98 \pm 0.04)$,
slope: $(13.34 \pm 0.003) \times 10^{-7}$,
$k = (66.70 \pm 0.05) \times 10^{-8}$ s^{-1},
$\Delta G^{\ddagger}_{323} = (117.4 \pm 0.01)$ kJ mol^{-1} (3)

We have carried out two other experiments of isomerization of **4** in DMSO-d_6 at 323 K, both in the presence of 5(6)-nitro-1*H*-benzotriazole (**5**) using two different **4**/**5** ratios, 1:2 and 1:1. In both cases a complex mixture of six compounds (**1**, **3**–**7**) was obtained (Scheme 2) that was monitored by NMR as a function of time (Fig. 4).

In 1967, Kamel et al. reported that the reaction between **5** and **2b** yielded a mixture of **6** (mp 185 °C, minor, about 10%) and **7** (mp 222 °C, major, about 90% in isolated products) without any amount of **8** (mp 170 °C, synthesized by an independent way).[3] This result, based only on chemical proofs, seemed doubtful to us because N-substitution reaction of **5** yields mainly 5-nitro derivatives.[25] Thus, either Kamel's assignment was wrong or the proportions were not correct. We repeated the reaction as described and found in the crude mixture by ^{1}H NMR that the proportions are 50% of **6**, 30% of **7**, and 20% of **8**. The melting points of **6**–**8** determined by DSC are somehow different from those described by Kamel et al.[3]

In our isomerization experiments of **4** in the presence of 5(6)-nitro-1*H*-benzotriazole (**5**), the composition depends on the stoichiometry, but always consists in a mixture of **1**, **3**–**7** (without traces of **8**). This already establishes that the isomerization process is *intermolecular*. Considering only the four dinitrophenyl derivatives (**3**, **4**, **6**, and **7**) and the



Scheme 2. Compounds expected in the reaction between **4** and **5**.

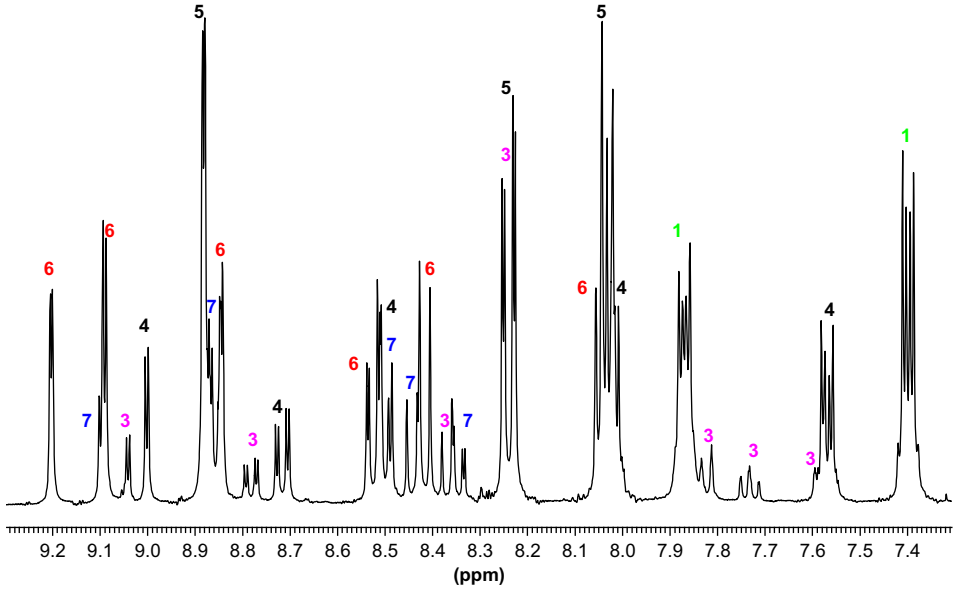


Figure 4. ^{1}H NMR spectrum showing the isomerization in DMSO-d_6 at 323 K of 2-isomer **4** in the presence of 5(6)-nitro-1*H*-benzotriazole (**5**) in a 1:2 ratio. Assignments (δ in ppm): 9.20 (H4, **6**), 9.10 (H3′, **7**), 9.09 (H3′, **6**), 9.04 (H3′, **3**), 9.00 (H3′, **4**), 8.88 (H4, **5**), 8.87 (H5′, **7**), 8.85 (H7, **7**), 8.84 (H5′, **6**), 8.78 (H5′, **3**), 8.72 (H5′, **4**), 8.53 (H7, **6**), 8.50 (H6′, **4**), 8.50 (H4, **7**), 8.44 (H6′, **7**), 8.42 (H6′, **6**), 8.37 (H6′, **3**), 8.34 (H5, **7**), 8.24 (H6, **5**), 8.24 (H4, **3**), 8.05 (H7, **6**), 8.03 (H7, **5**), 8.03 (H4, H7, **4**), 7.87 (H4, H7, **1**), 7.82 (H7, **3**), 7.73 (H6, **3**), 7.57 (H5, H6, **4**), 7.40 (H5, H6, **1**).

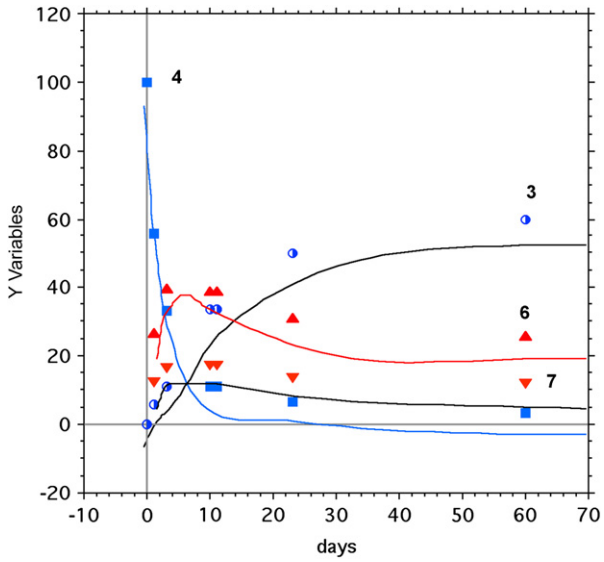


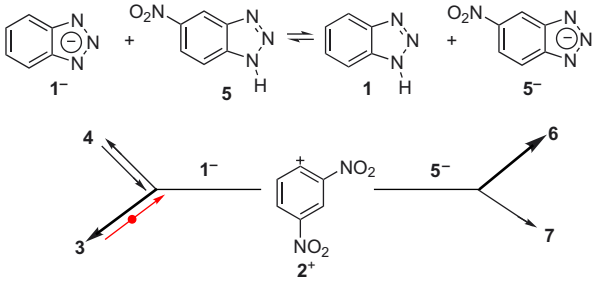
Figure 5. Evolution of the mixture of dinitrophenylbenzotriazoles. The Y variables are the percentages of the four components **3**, **4**, **6** and **7**.

case with a 1:2 ratio of **4** and **5**, the following plot is obtained (Fig. 5) corresponding to 60 days. All the data for both cases are given in Supplementary data.

Compound **4** (blue squares) disappears almost completely being not only transformed mainly into its isomer **3** (blue circles) but also into the two nitrobenzotriazole derivatives **6** (red triangles) and **7** (orange triangles). The **6**/**7** ratio is almost constant (2.28 in the 2:1 mixture and 2.23 in the 1:1 mixture) but the ratio [**3**]/[**4**] varies linearly with time (Eq. 4):

$$[\mathbf{3}]/[\mathbf{4}] = (0.304 \pm 0.007)t_{\text{days}},\ n = 7,\ r^2 = 0.997 \qquad (4)$$

The fact that no **8** was formed in these studies (DMSO) while in our hands, the reaction of **2** and **5** (EtOH/AcONa) affords **8** is probably related to the different solvents used or to the arylating agent, **2** or $\mathbf{2}^+$ (Scheme 3). The same reason could account for the ratio of **6**/**7**, in the first case is 1.67 (50:30) while in the cross-experiments is 2.25.



Scheme 3. The isomerization experiments, all species solvated by DMSO-d_6. The red arrow with the red point corresponds to a not observed process.

The reaction of 1-halo-2,4-dinitrobenzenes **2** (there is no visible effect of the halogen) with benzotriazole **1** depends on the nature, neutral **1** or anion $\mathbf{1}^-$, of the azole as well as on the solvent. With neutral benzotriazole, the solvent effects summarized in Table 1 (we have assumed a 98:2 mixture of **3**/**4** for the experiments in toluene and xylene where only **3** was isolated) can be analyzed as depending on the polarity and the acidity of the solvent, Reichardt's E_N^T and Swain's A_j:[26]

$$[\mathbf{3}]/[\mathbf{4}]\ \text{ratio} = (50 \pm 2) - (244 \pm 18)E_N^T + (170 \pm 20)A_j,$$
$$n = 8,\ r^2 = 0.989 \qquad (5)$$

Eq. 5 shows that the polarity of the solvent increases the amount of the 2-substituted isomer **4** while the acidity favors the 1-substituted isomer **3**. These conclusions are related to the tautomerism of benzotriazole [the 1(3)*H*-tautomer is much more stable than the 2*H* one][27] and to the acid–base equilibrium between benzotriazole **1** and its conjugated anion $\mathbf{1}^-$. The problem is complicated by the fact that both the 1*H*-tautomer and the anion can yield the two isomers. Katritzky and Wu assumed that the solvent polarity breaks down the hydrogen bonds of the 1*H*-benzotriazole dimer that shields the 2-position, favoring the 2-substituted isomer.[6] The acidity could shift the equilibrium between **1** and $\mathbf{1}^-$ and thus avoiding the reactivity of the anion, which according to entry 5 of Table 1, affords only **4**. Entry 6 (PTC, both isomers formed) corresponds to a reflux in toluene in the presence of K_2CO_3 plus a quaternary ammonium salt and thus is not a typical reaction of $\mathbf{1}^-$.[8] Entries 7–9 correspond to the exclusive formation of **3** although some of them uses DMF as solvent,[9] PTC and MW,[10] and ionic liquids.[11]

The isomerization experiments, without and with nitrobenzotriazole, correspond to the species and the relationships between themselves are represented in Scheme 3.

In DMSO-d_6 or DMF-d_7 solutions, compound **4** dissociates, even in a small amount, to benzotriazolate anion $\mathbf{1}^-$ and to the dinitrophenyl cation $\mathbf{2}^+$. In a less polar solvent, like $CDCl_3$, the dissociation does not occur and **4** is stable. In the absence of **5**, the cation $\mathbf{2}^+$ reacts with $\mathbf{1}^-$ to afford **4** since the 2-position of the anion is the most reactive. But, although less reactive, the 1(3)-position also react to yield **3** and slowly the quantity of **3** increases because **3** is not dissociated into $\mathbf{1}^-$ and $\mathbf{2}^+$. This kinetic stability of **3** compared to **4** is not necessarily related to its greater thermodynamic stability (Table 6). Note that the isomerization of **4**→**3** is not complete and an equilibrium is reached that is solvent dependent. However, in the presence of nitrobenzotriazole **5** almost all **4** disappears. Another important observation is that at 323 K the reaction in DMF is eight times faster than in DMSO and affords much more **3**, a fact probably related to the E_N^T values of both solvents (0.386 and 0.444) and the already noted observation that a decrease in polarity increases the amount of **3** (Eq. 5).

In the presence of nitrobenzotriazole **5** there should be an equilibrium with $\mathbf{1}^-$ that leads to $\mathbf{5}^-$ (Scheme 3). This last one would react with $\mathbf{2}^+$ to afford **6** (major) and **7** (minor). This is in contradiction with Kamel et al.[3] who reported that the reaction of **2a** with **5** (EtOH/AcOEt) affords mainly **7** (the ratio of isolated compounds **6**/**7** is 1:9). Most probably their assignment, based on chemical proofs, is erroneous; for instance, the reaction of **5** with picryl chloride (EtOH/AcOEt) yields a mixture of both picryl isomers in a ratio 44% of 6-nitro and 56% of 5-nitro.[28]

3. Conclusive remarks

All the previous reports compiled in Table 1, on the reaction between 1*H*-benzotriazole (**1**) and 1-halo-2,4-dinitrobenzenes (**2**) represented in Scheme 1, have based their explanation about the **3/4** ratios on kinetic effects. Nobody has considered that **4** could be formed just to isomerize into **3**. For instance, Beletskaya et al.[8] observed that longer reaction times increase the proportion of **3**. Isomerizations could have occurred under microwave irradiation,[10] or with the use of ionic liquids as solvents,[11] thus explaining the observed regioselectivity.

The fact that *N*-substituted benzotriazoles (like most azoles) can isomerize has been known for long time but they concern substituents like *N*-(*N*′,*N*′-dialkylaminomethyl) that are easy to cleave and be rapidly equilibrated: the equilibrium of [1-isomer]/[2-isomer] is 5.5 in $CDCl_3$ and >9 in DMSO.[29] However, no example is known of isomerization of an aryl group.

Minkin et al.[29,30] reported that no N,N-migration of a 2,4,6-trinitrophenyl (picryl) group was observed by ^{1}H NMR in solutions of 1-picryl-3,5-dimethylpyrazole in nitrobenzene even at 445 K, that is, the energy barrier $\Delta G^{\ddagger}_{445}$ is higher than 100 kJ mol^{-1}, confirming that dissociating solvents, like DMSO or DMF, are necessary to cleave the N−C bond.

4. Experimental

4.1. Synthesis and DSC melting points

Compounds **3** and **4** were prepared according to Wilshire's experimental conditions and separated by column chromatography over silica gel using a mixture of chloroform/hexane (99:1).[1] The reaction of 1-chloro-2,4-dinitrobenzene and 5(6)-nitrobenzotriazole in the conditions reported by Kamel et al. (1-chloro-2,4-dinitrobenzene in EtOH/AcONa at reflux)[3] affords a mixture of 1-(2′,4′-dinitrophenyl)-5-nitro-1*H*-benzotriazole (**6**), mp 189.8 °C, lit. mp 185 °C,[3] 1-(2′,4′-dinitrophenyl)-6-nitro-1*H*-benzotriazole (**7**), several melting and phase transitions around 220 °C, lit. mp 222 °C,[3] and 2-(2′,4′-dinitrophenyl)-5-nitro-2*H*-benzotriazole (**8**), mp 195.9 °C, lit. mp 170 °C.[3]

Melting points were determined by DSC on a Seiko DSC 220C connected to a Model SSC5200H Disk Station. The heating rates were 5° per minute with N_2 as the purge gas.

4.2. NMR measurements

4.2.1. Solution. The spectra were recorded on a Bruker DRX 400 (9.4 T, 400.13 MHz for ^{1}H, 100.62 MHz for ^{13}C, and 40.56 MHz for ^{15}N) spectrometer with a 5-mm inverse-detection H−X probe equipped with a *z*-gradient coil at 300 K. Chemical shifts (δ in ppm) are given from internal solvent, DMSO-d_6 2.49 for ^{1}H and 39.5 for ^{13}C, and for ^{15}N, nitromethane (0.00) was used as external references. Typical parameters for ^{1}H NMR spectra were spectral width 3100–3900 Hz, pulse width 7.5 μs, and resolution 0.19–0.24 Hz per point. Typical parameters for ^{13}C NMR spectra were spectral width 13,800–20,600 Hz, pulse width 10.6 μs, and resolution 0.42–0.63 Hz per point; WALTZ-16 was used for broadband proton decoupling; the FIDS were multiplied by an exponential weighting (lb=1 Hz) before Fourier transformation. 1D ^{15}N NMR was acquired using inverse gated decoupling and typical parameters were spectral width 14,368 Hz, pulse width 28.5 μs, relaxation delay 30 s, and resolution 0.44 Hz per point; WALTZ-16 was used for proton decoupling; the FIDS were multiplied by an exponential weighting (lb=2 Hz) before Fourier transformation. 2D (^{1}H−^{1}H) gs-COSY and inverse proton detected heteronuclear shift correlation spectra, (^{1}H−^{13}C) gs-HMQC, (^{1}H−^{13}C) gs-HMBC, and (^{1}H−^{15}N) gs-HMBC, were acquired and processed using standard Bruker NMR software and in non-phase-sensitive mode and the NOESY experiment was acquired with a mixing time of 1100 ms. Gradient selection was achieved through a 5% sine truncated shaped pulse gradient of 1 ms.

4.2.2. Solid state. ^{13}C (100.73 MHz) and ^{15}N (40.60 MHz) CPMAS NMR spectra were obtained on a Bruker WB 400 spectrometer at 300 K using a 4 mm DVT probehead. Samples were carefully packed in a 4-mm diameter cylindrical zirconia rotor with Kel-F end-caps. Operating conditions involved 3.2 μs 90° ^{1}H pulses and decoupling field strength of 78.1 kHz by TPPM sequence. ^{13}C spectra were originally referenced to a glycine sample and then the chemical shifts were recalculated to Me_4Si (for the carbonyl atom δ (glycine)=176.1 ppm) and ^{15}N spectra to $^{15}NH_4Cl$ and then converted to nitromethane scale using the relationship: δ ^{15}N (nitromethane)=δ ^{15}N(ammonium chloride)−338.1 ppm. The typical acquisition parameters for ^{13}C CPMAS were: spectral width 40 kHz; recycle delay 5 s for **3** and 60 s for **4**; acquisition time 30 ms; contact time 2 ms; and spin rate 12 kHz. And for ^{15}N CPMAS were: spectral width 40 kHz; recycle delay 5 s for **3** and 60 s for **4**; acquisition time 35 ms; contact time 9 ms; and spin rate 6 kHz.

4.3. Theoretical calculations

Energy calculations were carried out at the hybrid Becke B3LYP/6-31G** level 1[31–33] with basis sets of Gaussian-type functions[34] within the Windows Titan 1.0.5 package and include zero point energy (ZPE) corrections. Starting geometries for the calculations were the optimized ones obtained at the HF/6-31G** level. In all cases the final geometries really correspond to the minima as no imaginary frequencies appear. GIAO/B3LYP/6-31G* absolute shieldings calculations were carried out with the Gaussian 03 package.[35]

4.4. Kinetic experiments

4.4.1. Experiment 1. Compound **4** (40.2 mg), solvent DMSO-d_6 (0.75 mL, 0.1879 M), T=295 K, from 58,140 s to 168 days, 22 measures. Assuming that the final mixture contains 79.18% of **4** (20.82% of **3**), a_0=0.1879, equilibrium=0.7918, x_e=0.0391208, removing the first point and the latter one that corresponds to the equilibrium:

$$\ln\left[x_e/x_e - x\right] = \left(1.22 \pm 0.11\right) + \left(3.63 \pm 0.25\right) \times 10^{-7} t_s,$$
$$n = 20,\ r^2 = 0.922,\ k = \left(7.56 \pm 0.52\right) \times 10^{-8}\ \mathrm{s}^{-1} \quad (6)$$

4.4.2. Experiment 2. Compound **4** (40.2 mg), solvent DMSO-d_6 (0.75 mL, 0.1879 M), T=323 K, from 18,000 s

to 109 days, 17 measures. Assuming that the final mixture contains 84.17% of **4** (15.83% of **3**), a_0=0.1879, equilibrium=0.8417, x_e=0.0297446, removing the first point and the latter one that corresponds to the equilibrium:

$$\ln\left[x_e/x_e - x\right] = \left(1.14 \pm 0.07\right) + \left(5.16 \pm 0.25\right) \times 10^{-7} t_s,$$
$$n = 15,\ r^2 = 0.971,\ k = \left(8.17 \pm 0.40\right) \times 10^{-8}\ \mathrm{s}^{-1} \quad (7)$$

4.4.3. Experiment 3. Compound **4** (40.2 mg), solvent DMF-d_7 (0.75 mL, 0.1879 M), T=323 K, from 64,800 s to 45 days, 12 measures. Assuming that the final mixture contains 50.00% of **4** (50.00% of **3**), a_0=0.1879, equilibrium=0.5000, x_e=0.093950, removing the first point and the latter one that corresponds to the equilibrium:

$$\ln\left[x_e/x_e - x\right] = \left(0.98 \pm 0.04\right) + \left(13.34 \pm 0.003\right) \times 10^{-7} t_s,$$
$$n = 10,\ r^2 = 0.996,\ k = \left(66.70 \pm 0.05\right) \times 10^{-8}\ \mathrm{s}^{-1} \quad (8)$$

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Supplementary data

Supplementary data associated with this article can be found in the online version, at doi:10.1016/j.tet.2007.02.083.

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