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1-(NITROSOAMINO)BENZIMIDAZOLES CONTAINING ELECTRON-ACCEPTOR SUBSTITUENTS AT THE AMINE NITROGEN. THEORETICAL AND EXPERIMENTAL INVESTIGATION OF CONFORMATIONAL MOBILITY

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*The previously unknown 1-(N-nitrosoallylamino)- and 1-(N-nitrosopropargylamino)benzimidazoles have been synthesized and they exist in solution as a mixture of the E- and Z-conformers due to hindered rotation around the N–N(O) bond. The activation energies for the $E \rightleftarrows Z$ transition in these compounds and for the model N-benzyl analog have been determined by a dynamic ^{1}H NMR method. With a view to studying the effect of a substituent at the amino nitrogen on the $E \rightleftarrows Z$ isomerization we have carried out 3-21G and 6-31G** type ab initio calculations of the stable conformers of a series of N-nitrosohydrazines.*

Keywords: 1-(nitrosoamino)benzimidazoles, nitrosohydrazines, dynamic ^{1}H NMR, $E \rightleftarrows Z$ isomerization, quantum-chemical calculations.

The N-nitroso derivatives **2a-e** have recently been synthesized by us *via* the nitrosylation of the 1-(alkylamino)benzimidazoles (**1a-e**) [1] and these proved to be the first recorded representatives of N-(nitrosoamino)azoles (Scheme 1). It turns out that the given compounds exist in solution as a mixture of the *E*- and *Z*-forms, the ratio of which depends strongly on the nature of the solvent and the substituent R. An increase in the polarity of the medium and increase in the volume of the radical R raises the relative content of the more polar and sterically less hindered *Z*-conformer. It was of interest that, in the crystalline state as revealed by X-ray analysis, compound **2a** exists only as the *Z*-form [1]. Using dynamic ^{1}H NMR spectroscopy it was found that the values of the free energy of activation ($\Delta G^{\neq}$) and enthalpy of activation ($\Delta H^{\neq}$) for the $E \rightleftarrows Z$ transition in compound **2a** are 18.0 and 16.1 kcal/mol respectively (Table 1).

In continuation of these investigations we now report the synthesis of the N-allyl- and N-propargyl substituted 1-(nitrosoamino)benzimidazoles. It is proposed that the introduction of even such weakly electron acceptor groups decreases the order of the N–N(O) bond and thus leads to a lowering of the barrier to $E \rightleftarrows Z$ isomerization. In addition, this proposal was tested by of quantum-chemical calculations for a series of model N-nitrosohydrazines.

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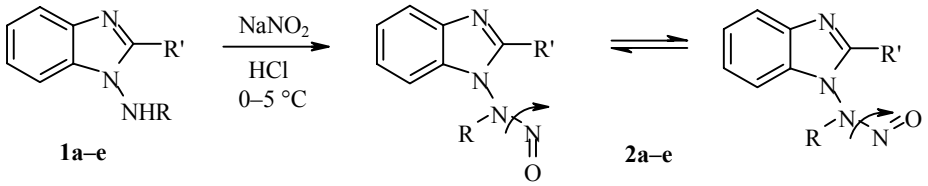
TABLE 1. *Ab Initio* Calculations of the Total Energy (E), Dipole Moments (μ), N^1–N^2 (l_1) and N^1–N(O) (l_2) Bond Lengths for the Potential Energy Surface (PES) Stable Conformers of Compounds **5-8**

Com-pound	Basis	E, a. u.	μ, D	l_1, Å	l_2, Å
Z-**5**	3-21G	-238.45462	2.2	1.413	1.344
	6-31G**	-239.83463	2.3	1.378	1.306
E-**5**	3-21G	-238.45036	3.0	1.405	1.345
	6-31G**	-239.83062	3.0	1.374	1.306
Z'-**5**	3-21G	-238.44478	4.8	1.390	1.364
	6-31G**	-239.02006	5.0	1.370	1.310
E'-**5**	3-21G	-238.44655	4.8	1.394	1.352
	6-31G**	-239.82776	4.8	1.370	1.310
Z-**6**	3-21G	-329.64629	3.7	1.414	1.401
E-**6**	3-21G	-329.64329	5.1	1.408	1.401
Z'-**6**	3-21G	-329.64118	3.3	1.401	1.422
E'-**6**	3-21G	-329.64160	4.2	1.403	1.409
Z-**7**	3-21G	-277.27209	2.6	1.418	1.335
E-**7**	3-21G	-277.26895	3.0	1.414	1.338
Z'-**7**	3-21G	-277.26152	5.1	1.399	1.359
E'-**7**	3-21G	-277.26491	5. 1	1.404	1.349
Z-**8**	3-21G	-406.11422	4.2	1.376	1.388
	6-31G	-408.22995	4.3	1.357	1.333
E-**8**	3-21G	-406.11395	2.7	1.372	1.377
	6-31G	-408.22962	2.9	1.352	1.328

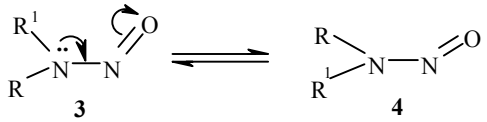
Scheme 1



1, **2** **a**, **e** R = Me, **b** R = Et, **c** R = *i*-Pr, **d** R = CH_2Ph; **a**–**d** R' = H; **e** R' = Me

Quantum-chemical Study of the Conformations of N-Nitrosohydrazines. A large volume of work has recently concerned the electronic structure and isomerization of N-nitrosoamines [2-4] due to the biological activity of this class of compound [5]. The partial double bond in the p-π conjugated N–N(O) fragment results in hindered rotation around the N–N bond [6, 7], as a result of which the N-nitrosoamines exist in solution as a pair of stable conformers **3** and **4** (Scheme 2).

Scheme 2



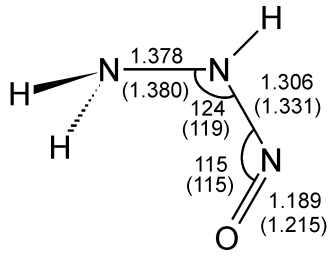


Fig. 1. Geometrical parameters for the N-nitrosohydrazine molecule **5** from 6-31G** type *ab initio* calculations (bond lengths in Å, angles in degrees) and experiment [1] (number in brackets).

In aliphatic nitrosoamines the barrier to rotation ($\Delta G^{\neq}$) around the N–N bond comes to 23 kcal/mol [8-10]. In their cyclic analogs $\Delta G^{\neq}$ depends on the size of the ring and varies in the range from 19.8 (N-nitrosoazetidine) to 22.7 kcal/mol (N-nitrosopiperidine) [8, 10]. In N-nitrosoarylamines the barrier to rotation, as might be expected, shows a tendency to decrease [11] provided that this is not hindered by steric factors [12].

A study of the mechanism of the $E \rightleftarrows Z$ isomerization in systems **2** was carried out using HF/3-21G, HF/6-31, and HF/6-31** type *ab initio* type calculations with full optimization of the geometrical parameters *via* the GAUSSIAN-94 program [13]. In the initial step of the investigation of the $E \rightleftarrows Z$ isomerization the N-nitrosohydrazine **5** was studied as the simplest model of a 1-(nitrosoalkylamino)benzimidazole **2**. The results of 6-31G** type calculations are given in Fig. 1 and agree well with the corresponding X-ray data for compound **2e** [1].

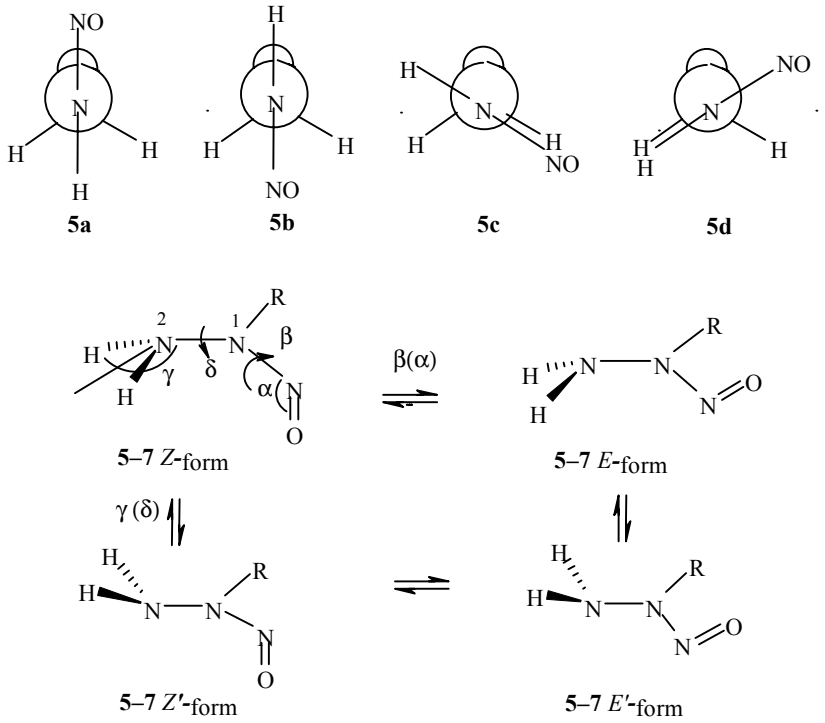
According to the calculations, N-nitrosohydrazine can be stabilized in the form of non-equivalent *gauche* (**5a**, **5b**), *syn* (**5c**), and *anti* (**5d**) conformers. However, the actual minima in the potential energy surface (PES) (all individual Hess values positive, $\lambda > 0$) correspond to only conformers **5a** and **5b** whereas for the *syn*- and *anti*-isomers the population of negative individual values have $\lambda > 1$ and, consequently, they do not correspond to minima on the PES.

The calculations also show that in the N-nitrosohydrazine **5** the substituted nitrogen centre N^1 is planar (close to sp^2-hydridized) as a result of which the possibility arises of the existence of four different *gauche* conformers (Scheme 3, Table 1) which differ in the structure of the N–N(O) fragment. All of these forms (*Z*, *E*, *Z*', *E*') are stable on the PES while the most stable is the *Z*-form.

In its structure and orbital situation the three-component fragment N–N(O) fragment behaves similarly to the isoelectronic allyl anion. This permits both delocalization of the lone electron pair of atom N^1 and its transformation into the "allyl-like" part of the molecular orbitals, thus sharply increasing the multiplicity of the N^1–N(O) bond. As a result of this, the barrier to rotation around the N^1–N(O) bond increases to 18.5 kcal/mol (6-31G** type calculation). According to data from dynamic ^{1}H NMR spectroscopy the barrier for compound **1a** is 18.0 kcal/mol [1]. For comparison, the calculated barrier to pyramidal inversion (corresponding to a change in the angle γ) is only 6 kcal/mol (Table 2).

Along with the routes of $E \rightleftarrows Z$ isomerization are the planar inversion around the angle α or rotation about angle δ, however these process are energetically much less favored according to the calculated data. Thus the $E \rightleftarrows Z$ isomerization in the model N-nitrosohydrazine **5**, as a consequence of the PES system (Fig. 3), occurs as a complex procedure combining the two processes of rotation around the N^1–N(O) bond and pyrimidal low-barrier inversion at the amine nitrogen atom.

Scheme 3



5 R = H, **6** R = CN, **7** R = Me

Isomerization of Substituted N-Nitrosohydrazines and N-(nitrosoamino)imidazoles. We have further investigated the effect on the mechanism of the $E \rightleftarrows Z$ isomerization of a substituent at the nitrogen atom which bears the N-nitroso group. The N-cyano- (**6**) and N-methyl-N-nitrosohydrazines (**7**) were chosen as two model compounds.

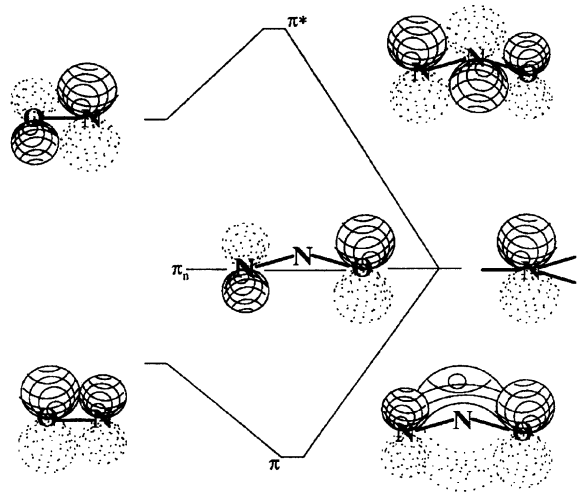


Fig. 2. π-Molecular orbitals for N-nitrosohydrazine **5**.

TABLE 2. Activation Barriers $\Delta E^{\neq}$ for the Plane of Inversion (Angle α), Rotation Around Bonds (Angles β, δ), and Pyramidal Inversion (Angle γ) in the N-Nitrosohydrazine (**5**) and 1-(Nitrosoamino)imidazole (**8**) Molecules

Compound	Basis	Angle	$\Delta E^{\neq}$, kcal/mol	Compound	Basis	Angle	$\Delta E^{\neq}$, kcal/mol
5	6-31G**	α	6.0	**8**	3-21G	β	13.1
		β	18.5			δ	8.5
		γ	40.2				

It was found that the introduction of a CN electron-acceptor group at the N^1 atom (compound **6**) leads to a decrease in the multiplicity of the N^1–N(O) bond and to an increase in its length (Table 1) when compared with the unsubstituted system **5**. At the same time, in the N-methyl substituted compound **7** the central bond is conversely strengthened. Hence the acceleration of the $E \rightleftarrows Z$ isomerization is favored by electron-acceptor substituents on atom N^1. Moreover, it is apparent that the barrier to $E \rightleftarrows Z$ isomerization is associated with a decrease in the difference in energy of the isomers (Table 1).

In addition to this we have studied the effect of including the N-nitrosoamino fragment in an aromatic imidazole system (compound **8**), the closest to the experimentally studied 1-(nitrosoalkylamino)benzimidazoles **2**. By contrast with the N-nitrosohydrazine **5**, the only associated rotation around the N^1–N(O) bond in the system **8** is a rotation around angle δ (about the N^1–N^2 bond), since the possibility of pyramidal inversion is absent due to the planar structure of the imidazole unit (Scheme 4). Hence, as might be expected, the length of the N^1–N^2 bond increases and this leads in both the *Z*- and *E*-isomers to a significant lowering of the topomerization activation barrier (according to 3-21G calculated data $\Delta E^{\neq}$ = 13.1 kcal/mol).

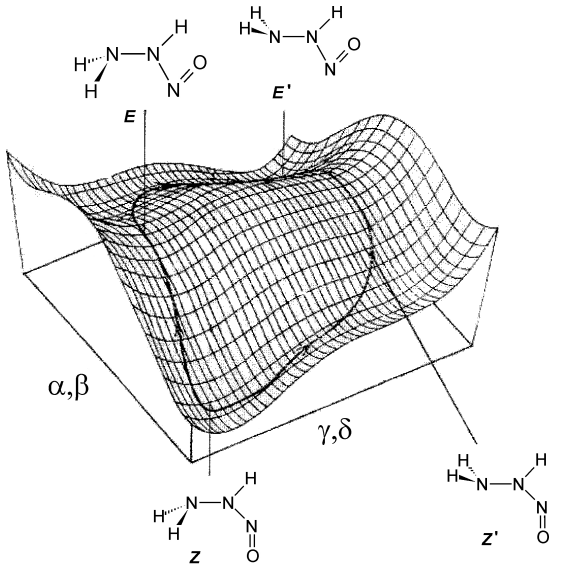
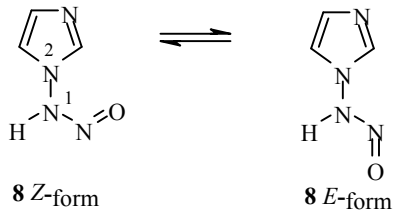


Fig. 3. General view of the PES for N-nitrosohydrazine **5** from *ab initio* calculations.

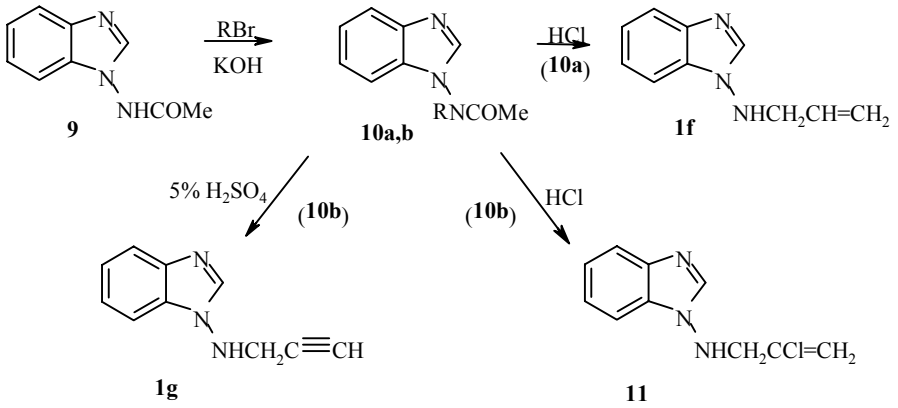
Scheme 4



8 *Z*-form **8** *E*-form

Experimental Study of the *E* ⇄ *Z* Isomerization of Novel 1-(N-nitrosoalkylamino)-benzimidazoles. Based on the theoretical prediction given above we studied experimentally the *E* ⇄ *Z* isomerization in the previously unknown 1-(N-nitrosoalkylamino)benzimidazoles **2f,g**. The 1-(N-acetylamino)benzimidazole (**9**) was used as starting material and this was alkylated with allyl bromide or propargyl bromide in acetone in the presence of KOH to give the 1-(N-allyl-N-acetylamino)- (**10a**) and 1-(N-acetyl-N-propargylamino)benzimidazoles (**10b**) (Scheme 5).

Scheme 5



10 a R = $CH_2CH{=}CH_2$; **b** R = $CH_2C{\equiv}CH$

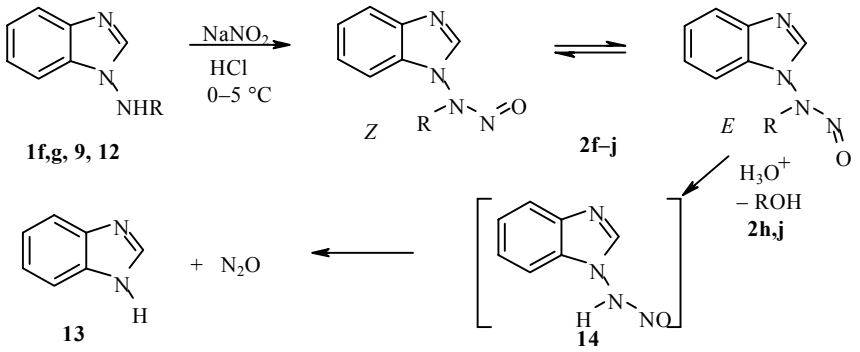
Hydrolysis of benzimidazole **10a** on refluxing in concentrated HCl gives a 70% yield of 1-(allylamino)benzimidazole (**1f**). The latter is also formed by treatment of compound **9** with allyl bromide in DMSO in the presence of KOH. Evidently, in these conditions, ready hydrolysis of the acetyl group follows the introduction of the allyl group. Upon heating in concentrated HCl compound **10** is converted to 1-[(2-chloroallyl)amino]benzimidazole (**11**) in 93% yield, i.e. addition of 1 mole equivalent of HCl occurs in addition to the fission of the acetyl group. The 1-(propargylamino)benzimidazole (**1g**) can be prepared by carrying out the hydrolysis of compound **10b** in 5% sulfuric acid.

Treatment of compounds **1f,g** with nitrous acid gives moderate yields of the 1-(N-nitrosoalkylamino)benzimidazoles **2f,g**. Compound **11** reacts with nitrous acid to give a complex mixture of unstable materials not amenable to separation.

Additionally, we have carried out an attempt to synthesize the 1-(N-nitrosoacylamino)benzimidazoles (**2h,i**), expecting to obtain compounds with strongly electron-acceptor groups at the amine nitrogen. However, the nitrosylation of 1-(acetylamino)- (**9**) or 1-(tosylamino)benzimidazoles (**12**) gave the unsubstituted benzimidazole **13** as the only reaction product. Very likely, the initially obtained nitroso compounds with two strongly electron-acceptor substituents at the nitrogen atom (**2i,j**) are unstable and are rapidly hydrolyzed to

nitrosoamine **14** and this decomposes to the benzimidazole and the nitrogen oxide (Scheme 6). The previously unknown compound **12** was prepared by fusing 1-aminobenzimidazole with p-toluenesulfonyl chloride at 100-110°C.

Scheme 6



1, 2 f R = $CH_2CH{=}CH_2$; **g** R = $CH_2C{\equiv}CH$; **2i, 9** R = COMe; **2j, 12** R = *n*-Ts

At room temperature, the ^{1}H NMR spectra of the nitrosoamines **2f,g** show doubling of all the proton signals, the assignment of which were carried out as described before for compounds **2a-e** [1]. By dynamic ^{1}H NMR in DMSO-d$_6$ the free energies of activation $\Delta G^{\neq}$ of the $E \rightleftarrows Z$ transition for compounds **2f,g** and also for the N-benzyl analog **2d** synthesized previously [1] were determined. Figure 4 shows a view of the indicator signals (2-H and the N-alkyl groups). Increasing the temperature causes a broadening and then a coalescence of these signals. After cooling the spectrum reverts to its initial form.

According to Table 3, in the series **2a-2d-2f-2g** an increase in the electron acceptor property of the substituent R is accompanied by a decrease in the energy of activation ($\Delta G^{\neq}_{298}$) of the $E \rightleftarrows Z$ isomerization and this agrees with the trend obtained on the basis of calculations. In addition, the barrier to rotation remains sufficiently high so that both possible conformers are observed in solution under ordinary conditions.

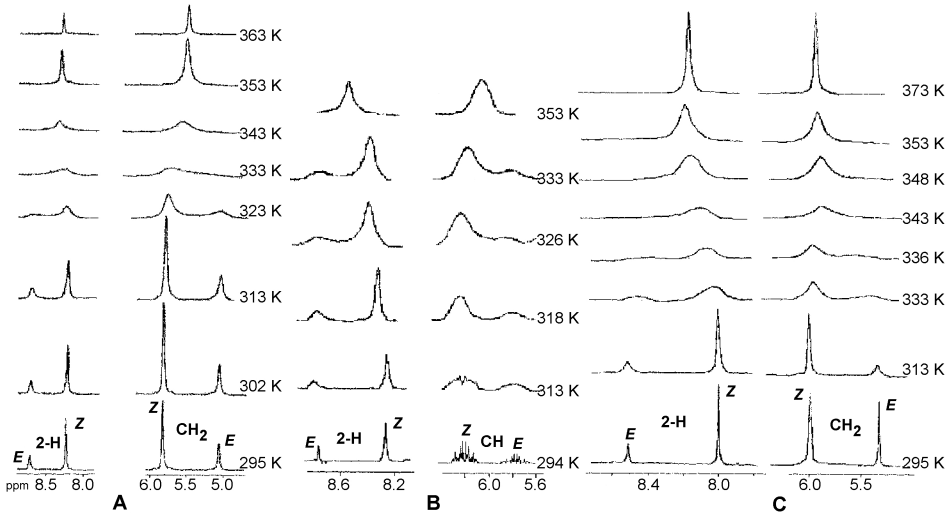


Fig. 4. View of the indicator signals (2-H and N-Alkyl) in the temperature dependant ^{1}H NMR spectra of compounds **2g** (A), **2f** (B), and **2d** (C) (DMSO-d$_6$).

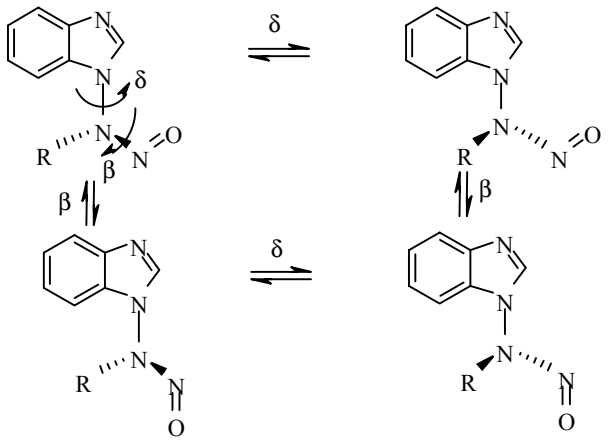
TABLE 3. Ratio of *E*- and *Z*-Conformers (DMSO-d6, 25°C) and Thermodynamic Parameters for the $E \rightleftarrows Z$ Isomerization in the Benzimidazoles **2**

Compound	Ratio of *E*- and *Z*-conformers, %	$\Delta G^{\neq}_{298}$ kcal/mol	$\Delta H^{\neq}$, kcal/mol
2a*	43/57	18.0	16.1
2d	25/75	17.23	24.9
2f	26/74	16.8	21.9
2g	33/67	16.7	21.6

* See communication [1].

Hence the basic conclusion of the experimental and theoretical study of system **2** shows that, on the whole, the $E \rightleftarrows Z$ isomerization of the N-nitrosoamines can only take place *via* cooperative processes, the components of which depend of the electronic structure of the system. For the N-nitrosohydrazines this mobility is described by the angles β and γ and for the N-(nitrosoamino)benzimidazoles it is based on the angles β and δ (Scheme 7, see also Table 2 and Fig. 3).

Scheme 7



EXPERIMENTAL

IR spectra for compounds **10a** and **2f** were recorded on a UR-20 instrument using vaseline oil and for compound **11** on a Specord M-40 for solutions in chloroform. The ^{1}H NMR spectra were obtained on a Bruker-250 instrument (250 MHz) for solutions in $CDCl_3$ or DMSO-d6. Monitoring of the reaction course and the purity of the obtained compounds was carried out using TLC on Al_2O_3 plates (Brockmann grade 4-5) with chloroform eluent and were developed with iodine vapor. Melting points for the synthesized compounds were determined on a PTP apparatus in sealed capillaries and were not corrected.

The change in free energy of activation $\Delta G^{\neq}$ was calculated according to the equation:

$$\Delta G^{\neq} = 4.57\ T\ (10.32 + 0.4343 \ln T/K) \cdot 10^{-3}$$

Rotational rate constants were determined according to the equations for slow exchange (1) and for rapid exchange (2):

$$K = 2\,(\Delta\nu_{1/2} - \Delta\nu^{0}_{1/2})\,, \qquad (1)$$

$$K = 2\pi\, p_A\, p_b\, \Delta\nu \frac{\left\{\frac{\Delta\nu^{0}_{1/2}}{\Delta\nu} + \frac{\Delta\nu_{1/2}}{\Delta\nu}\left[1 + 2\left(\frac{\Delta\nu_{1/2}}{\Delta\nu}\right)^2 - \left(\frac{\Delta\nu_{1/2}}{\Delta\nu}\right)^4\right]^{1/2}\right\}}{\left(\frac{\Delta\nu_{1/2}}{\Delta\nu}\right)^2 - \left(\frac{\Delta\nu^{0}_{1/2}}{\Delta\nu}\right)^2}\,, \qquad (2)$$

where $\Delta\nu$ is the maximum separation of the signals, $\Delta\nu^{0}_{1/2}$ the width of the signal at half-height in the absence of exchange, and $\Delta\nu_{1/2}$ is the width of the signal at half-height (in Hz) [14].

The change in free energy of activation at 25°C ($\Delta G^{\neq}_{298}$) was measured by a least squares approximation method.

The starting 1-aminobenzimidazole [15], 1-(acetylamino)benzimidazole **9** [16], and 1-(benzylamino)-benzimidazole **2d** [1] were prepared by known methods.

1-(N-Allyl-N-acetylamino)benzimidazole (10a). Finely powdered KOH (2.25 g, 0.04 mol) was added to a solution of compound **9** (7 g, 0.04 mol) in absolute acetone (220 ml) and the product was stirred for 15 min. Allyl bromide (3.3 ml, 0.04 mol) was added and the mixture was held for 4 h at room temperature. Acetone was distilled off, chloroform (20 ml) was added to the residue, the product was filtered to remove precipitated KBr, and the filtrate was passed through an Al_2O_3 column (l = 35 cm, d = 2.5 cm) using chloroform eluent. The fraction with R_f 0.6 was collected to give compound **10a** (6.6 g, 77%) as yellow oil. IR spectrum (liquid film), ν, cm^{-1}: 3100 (C–H_{arom}), 1700 (C=O), 1620, 1500 (ring). Found, %: C 70.27; H 6.30; N 19.33. $C_{12}H_{13}N_3O$. Calculated, %: C 66.96; H 6.09, N 19.52.

1-(Allylamino)benzimidazole (1f). A. A solution of compound **10a** (2.15 g, 0.01 mol) in HCl (15%, 10 ml) was refluxed for 2 h. After cooling it was neutralized by concentrated ammonia to pH 7-8. The reaction product was extracted with chloroform (3 x 10 ml) and the chloroform solution was passed through an Al_2O_3 column (l = 20 cm, d = 1.5 cm) using chloroform eluent. The fraction with R_f 0.35 was collected to give compound **1f** (1.2 g, 69%) as colorless crystals; mp 73-76°C (octane). IR spectrum (vaseline oil), ν, cm^{-1}: 3200 (NH), 3090 (C–H arom.), 1500 (ring). ^{1}H NMR spectrum ($CDCl_3$), δ, ppm, J (Hz): 3.8 (2H, d, ^3J = 6.31, NH~~CH~~$_2$); 5.0 (1H, br. s, NH, disappearing on deuteration); 5.10 (2H, m, =CH_2); 5.90 (1H, m, CH=); 7.31 (2H, m, 5-, 6-H); 7.48 (1H, m, 4-H); 7.75 (1H, m, 7-H); 7.95 (1H, s, 2-H). Found, %: C 69.67; H 6.56; N 24.00. $C_{10}H_{11}N_3$. Calculated, %: C 69.34; H 6.40; N 24.26.

B. Compound **9** (1.4 g, 8 mmol) was added to a solution of KOH (1.12 g, 0.02 mol) in DMSO (10 ml) and the product was stirred for 15 min. Allyl bromide (0.66 ml, 8 mmol) was added and the reaction mixture was stirred for 2 h at room temperature. After diluting with water (15 ml) the product was extracted with chloroform (3 × 10 ml). The chloroform solution was washed with water (2 × 10 ml) and then passed through an Al_2O_3 column (l = 20 cm, d = 1.5 cm) using chloroform eluent. The fraction with R_f 0.35 was collected to give compound **1f** (0.7 g, 51%) as colorless crystals; mp 72-75°C (octane).

1-(N-Acetyl-N-propargylamino)benzimidazole (10b). Finely powdered KOH (0.5 g, 9 mmol) was added to a solution of compound **9** (1.2 g, 6.8 mmol) in acetone (15 ml) and the product was stirred for 15 min. Propargyl bromide (0.45 ml, 6.8 mmol) was added and the reaction mixture was stirred for 2 h at room temperature. The acetone was distilled off, the residue was triturated with chloroform (15 ml), the solution was filtered and then passed thorough an Al_2O_3 column (l = 20 cm, d = 1.5 cm) using chloroform eluent. The fraction with R_f 0.65 was collected to give compound **10b** (0.85 g, 59%) as colorless crystals; mp 112-115°C

(octane). ^{1}H NMR spectrum ($CDCl_3$), δ, ppm, J (Hz): 1.90 (3H, s, $COCH_3$); 2.30 (1H, t, ^4J = 2.4, CH); 4.30 (1H, dd, ^4J = 2.4, ^2J = 17.5, CH_2); 5.05 (1H, dd, ^4J = 2.4, ^2J = 17.4, CH_2); 7.36 (3H, m, 4-, 6-H); 7.83 (1H, m, 7-H); 8.06 (1H, s, 2-H). Found, %: C 67.95, H 5.41; N 19.60. $C_{12}H_{11}N_3O$. Calculated, %: C 67.59; H 5.20; N 19.71.

1-(Propargylamino)benzimidazole (1g). A solution of **10b** (0.5 g, 2.3 mmol) was refluxed in H_2SO_4 (5%, 25 ml) for 1.5 h. With cooling, it was neutralized using concentrated ammonia to pH 7-8. The reaction product was extracted with chloroform (3 × 5 ml). The chloroform solution was passed through an Al_2O_3 column (l = 20 cm, d = 1.5 cm) using chloroform eluent. The fraction with R_f 0.35 was collected to give compound **1g** (0.35 g, 87%) as colorless crystals; mp 88-91°C (octane). ^{1}H NMR spectrum ($CDCl_3$), δ, ppm, J (Hz): 2.40 (1H, t, ^4J = 2.4, CH); 3.90 (2H, s, $–CH_2$); 5.10 (1H, br. s, NH, disappearing upon deuteration); 7.35 (2H, m, 5-, 6-H); 7.50 (1H, m, 4-H); 7.78 (1H, m, 7-H); 8.10 (1H, s, 2-H). Found, %: C 70.39; H 5.02; N 24.66. $C_{10}H_9N_3$. Calculated, %: C 70.16, H 5.20; N 24.54.

1-[(2-Chloroallyl)amino]benzimidazole (11). A solution of compound **10b** (0.4 g, 1.9 mmol) in HCl (5%, 15 ml) was refluxed for 1.5 h. With cooling, it was neutralized using concentrated ammonia to pH 7-8. The reaction product was extracted with chloroform (3 × 5 ml). The chloroform solution was passed through an Al_2O_3 column (l = 20 cm, d = 1.5 cm) using chloroform eluent. The fraction with R_f 0.45 was collected to give compound **11** (0.36 g, 93%) as a light yellow oil. IR spectrum ($CHCl_3$), ν, cm^{-1}: 3300 (NH), 2970 (C–H arom.) 1620, 1580, 1500 (ring). ^{1}H NMR spectrum ($CDCl_3$), δ, ppm, J (Hz): 3.90 (2H, d, ^3J = 2.8, $–CH_2$); 5.20 (1H, t, $^4J_{cis}$ = 0.7, $=CH_2$); 5.30 (1H, d, $^4J_{trans}$ = 1.7, $=CH_2$); 5.04 (1H, br. s, NH, disappearing upon deuteration); 7.30 (2H, m, 5-, 6-H); 7.50 (1H, m, 4-H); 7.78 (1H, m, 7-H); 8.10 (1H, s, 2-H). Found, %: C 58.07; H 5.03; Cl 17.32; N 20.38. $C_{10}H_{10}ClN_3$. Calculated, %: C 57.84; H 4.85; Cl 17.07; N 20.23.

General Method for Preparation of 1-(Nitrosoalkylamino)benzimidazoles (2). A solution of an equimolar amount of sodium nitrite in water was added dropwise to a solution of compound **1f** or **1g** (2%) cooled to -5°C at such a rate that the temperature did not exceed 0°C. The pale yellow mixture was held for 30 min at -5 to 0°C, after which it was neutralized with concentrated ammonia to pH 7-8 and the emulsion formed was extracted with chloroform (10 ml). The chloroform solution was passed through an Al_2O_3 column (l = 20 cm, d = 1.0 cm) using chloroform eluent. The fraction with R_f ~ 0.7 was collected. The chloroform was evaporated off and the residue evacuated to give compounds **2f,g** as oils which were used without additional purification.

1-(N-nitrosoallylamino)benzimidazole (2f) was prepared from compound **1f** (0.1 g, 0.58 mmol) as a pale yellow oil in 0.054 g (46%) yield. ^{1}H NMR spectrum ($CDCl_3$), δ, ppm: 4.61 (2H, br. s, $–CH_2$, E); 5.25 (6H, m, $–CH_2$ Z, CH_2= E, CH_2= Z); 5.65 (1H, m, –CH– E); 6.04 (1H, m, –CH– Z); 7.02 (1H, m, 4-H Z); 7.32 (5H, m, 4-, 6-H E, 5-, 6-H Z); 7.61 (1H, s, 2-H Z); 7.82 (2H, m, 7-H E, 7-H Z); 8.05 (1H, s, 2-H E). ^{1}H NMR spectrum (DMSO-d_6), δ, ppm J (Hz): 4.78 (2H, d, ^3J = 6.6, CH_2– E); 5.31 (6H, m, CH_2– Z, CH_2= E, CH_2= Z); 5.75 (1H, m, CH– E); 6.18 (1H, m, CH– Z); 7.30 (4H, m, 5-, 6-H E, 5-, 6-H Z); 7.40 (1H, m, 4-H Z); 7.56 (1H, m, 4-H E); 7.75 (1H, m, 7-H Z); 7.82 (1H, m, 7-H E); 8.20 (1H, s, 2-H Z); 8.73 (1H, s, 2-H E). Found, %: C 59.83; H 5.22; N 27.50. $C_{10}H_{10}N_4O$. Calculated, %: C 59.40; H 4.98; N 27.71.

1-(N-Nitrosopropargylamino)benzimidazole (2g) was prepared from compound **1g** (0.05 g, 0.3 mmol) as a light yellow oil (0.02 g, 34%). ^{1}H NMR spectrum (DMSO-d_6), δ, ppm: 3.67 (1H, br. s, CH– Z); 5.05 (2H, s, CH_2 E); 5.82 (2H, s, CH_2 Z); 7.36 (5H, m, 5-, 6-H Z 4-, 6-H E); 7.56 (1H, m, 7-H E); 7.80 (2H, m, 4-, 7-H Z); 8.23 (1H, s, 2-H Z); 8.73 (1H, s, 2-H E). Found, %: C 60.15; H 4.37; N 28.34. $C_{10}H_8N_4O$. Calculated, %: C 59.99; H 4.03; N 27.99.

1-(Tosylamino)benzimidazole (12). A mixture of 1-aminobenzimidazole (0.133 g, 1 mmol) and *p*-toluenesulfonyl chloride (0.191 g, 1 mmol) was held for 1 h at 100-110°C. After cooling, the melt was triturated with a mixture of methanol and diethyl ether (1:10, 10 ml) and the precipitate was filtered off to give compound **12** (0.168 g, 60%) as light grey crystals; mp 240-242°C (decomp.; from methanol). ^{1}H NMR spectrum (DMSO-d_6), δ, ppm, J (Hz): 2.39 (3H, s, CH_3); 5.60 (1H, s, NH); 6.96 (1H, m, 4-H) 7.16 (1H, dt,

^3J = 7.27, ^4J = 1.07, 5-H); 7.25 (1H, dt, ^3J = 7.27, ^4J = 1.05, 6-H); 7.38 (2H, d, ^3J = 7.93, 3'-, 5'-H); 7.60 (2H, d, ^3J = 8.23, 2'-, 6'-H); 7.65 (1H, m, 7-H); 8.23 (1H, s, 2-H). Found, %: C 58.88; H 4.29; N 14.46, S 10.97. $C_{14}H_{13}N_3O_2S$. Calculated, %: C 58.52; H 4.56; N 14.62; S 11.16.

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