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Synthesis and Some Properties of 1-(N-Nitrosoalkylamino)benzimidazoles[∂]

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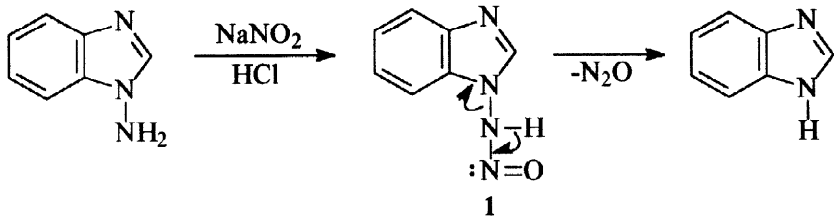
Abstract. 1-(N-Nitrosoalkylamino)benzimidazoles (**7a-e**) were prepared by nitrosation of the parent amines with nitrous acid. The NMR data revealed **7a-d** in solutions as mixtures of E and Z-isomers due to hindered rotation around the N-NO bond. 1-(N-Nitrosoisopropylamino)benzimidazole (**7e**) existed in solutions as a sole Z-isomer. The rotation barrier around the N-NO bond was estimated for **7a** by ^{1}H NMR dynamic spectroscopy. The molecular structure of 1-(N-nitrosomethylamino)-2-methylbezimidazole (**7d**) was confirmed by X-ray structural data. © 1998 Elsevier Science Ltd. All rights reserved.

Introduction

It is known that under the action of nitrous acid N-aminoazoles undergo fast and mild elimination of the amino group.[1] The process supposedly proceeds via a very labile N-nitrosoamine intermediate (e.g. **1**) followed by elimination of N_2O (Scheme 1). The readiness of this reaction favours an application of the N-amino group in azoles as a convenient blocking function in some preparations.[2]

Scheme 1



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Until recently, no data appeared on the reactivity towards nitrous acid of the secondary amino group attached to the heterocyclic nitrogen atom. In 1993, Japanese chemists reported that on treatment with nitrous acid, N-alkylaminopyridinium salts underwent deamination, whereas 1-alkylaminouracyls were converted into stable N-nitrosoalkylamino derivatives. [3] The main goal of the present research was to investigate the similar reaction in the benzimidazole series with special

[∂] Dedicated to Professor A.R.Katritzky on Occasion of his 70th Birthday

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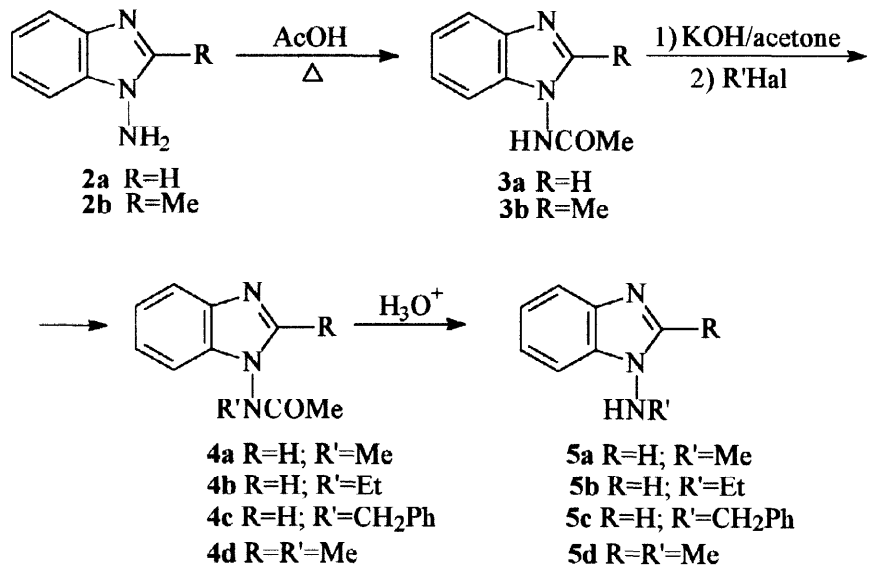
attention to structural peculiarities of the products, 1-(N-nitrosoalkylamino)benzimidazoles.

Synthesis of 1-(N-nitrosoalkylamino)benzimidazoles

1-Alkylaminobenzimidazoles (**5a-d**) were synthesized from 1-aminobenzimidazole (**2a**), or from the 2-methylsubstituted derivative (**2b**) as shown in Scheme 2. [4] 1-Isopropylaminobenzimidazole (**5e**) was obtained in a better yield by sodium borohydride reduction of 1-isopropylidenaminobenzimidazole (**6**) formed *in situ* from the amine **2a** and acetone (Scheme 3).

Scheme 2



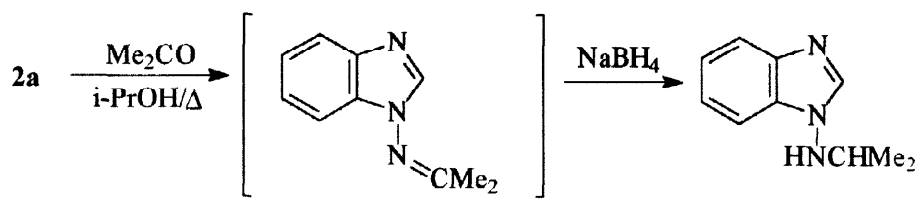
2a R=H
2b R=Me

3a R=H
3b R=Me

4a R=H; R'=Me
4b R=H; R'=Et
4c R=H; R'=CH_2Ph
4d R=R'=Me

5a R=H; R'=Me
5b R=H; R'=Et
5c R=H; R'=CH_2Ph
5d R=R'=Me

Scheme 3

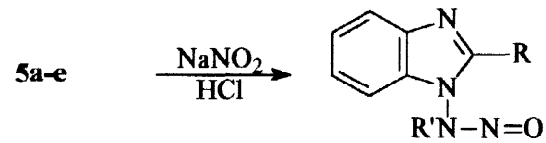


6 **5e**

We found that nitrosation of **5a-e** with HNO_2, generated from sodium nitrite in hydrochloric acid, was similar to the reaction of primary amino derivatives, and proceeded under mild conditions (-5 - 0 °C) to give the corresponding 1-(N-nitrosoalkylamino)benzimidazoles (**7a-e**) in 50-60 % yields (after chromatographic purification) (Scheme 4). Compounds **7a-c,e** were obtained as pale yellow oils and slowly decomposed upon storage, whereas **7d** was isolated as stable yellowish crystals with m.p. 76-78

°C. None of the compounds **7a-e** had characteristic bands in the IR spectra. The electron impact mass-spectrum of nitrosoamine **7a** did not reveal the molecular ion, probably due to its instability. Instead, the highest intensity peak belonged to a fragment formed by elimination of NO from the molecular ion.

Scheme 4



7a R=H; R'=Me
7b R=H; R'=Et
7c R=H; R'=CH_2Ph
7d R=Me; R'=Me
7e R=H; R'=i-Pr

X-Ray Crystallography

Like other N-nitrosoamines, [5,6] compounds **7a-e** can theoretically exist in *Z*-(**8a**) and *E*-(**8b**) forms due to restricted rotation around the N-N(O) bond. This is a result of conjugation of the nitrogen atom of the amino group, and the nitroso group leading to a significant contribution of 1,3-dipolar resonance structures of type **8a`** or **8b`**. For confirmation of this assumption, the X-ray crystallographic analysis data for at least one of the studied nitrosoalkylamines was important. These data were obtained for compound **7d** (Figure 1).

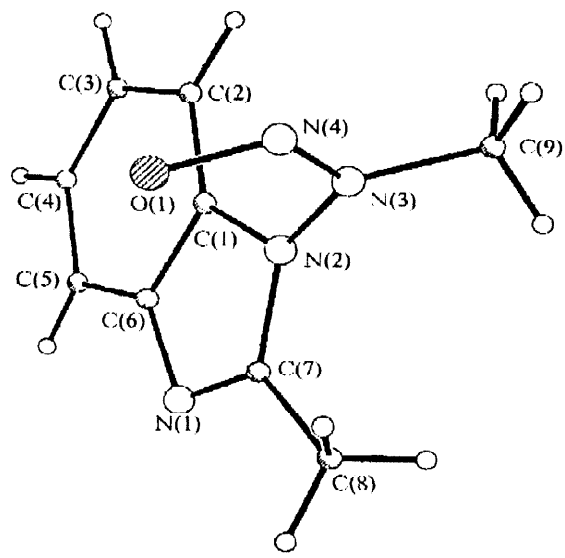
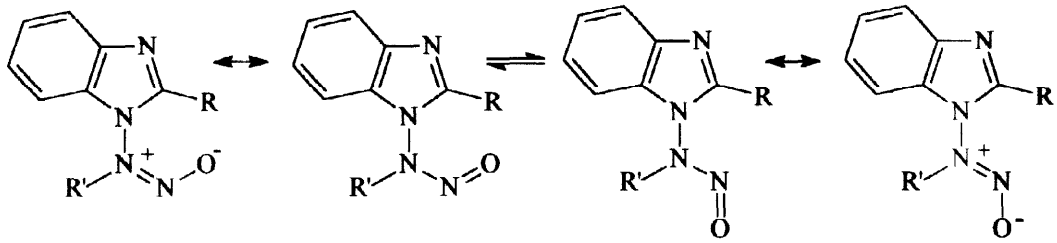


Figure 1. Molecular structure of **7d** with crystallographic numbering scheme.

Table 1 contains a selection of geometrical parameters. The structure **7d** is characterised by the following key features: *(i)* The molecule consists of two almost perfect planar systems - the benzimidazole fragment, and nitrosomethylamino group. The dihedral angle between these two planes [C(1), C(2), C(3), C(4), C(5), C(6), C(7),N(1), N(2) and N(2), N(3), N(4), C(9), O(1)] is equal to 88.58 (0.08)°. *(ii)* The nitrogen atom of the substituted amino group is purely in the geometry of sp^2-

hybridization [sum of valence angles at N(2) is equal to 360.0 °], unlike 1-aminobenzimidazole where the nitrogen atom of the amino group is in a configuration of sp^3-hybridization.[7] Obviously, such a difference is the result of conjugation of the amine group and nitroso groups in **7d** as described above. A significant similarity between the amino group in **7d** and 1-aminobenzimidazole is that in both molecules a lone electron pair of the nitrogen atom eclipses the heterocycle ring plane. *(iii)* N-Nitrosomethylamino fragment has the *Z*-configuration. Thus, the molecular structure of **7d** resembles 1-formamidoindazole and 1-formamidopyrazole.[8] This is quite logical since nitrosoamino and formamido groups are isoelectronic.



8a' **8a (Z-form)** **8b (E-form)** **8b'**

NMR Spectra and Rotational Isomerism

The most important peculiarities of ^{1}H NMR spectra of compounds **7a-d** (**7e** - is an exception, see below) are double sets of all signals, and dependence of their relative intensities on the nature of a solvent and on the size of the N-alkyl group (Figure 2, Table 2). Obviously, this is a result of coexistence of *E*- and *Z*-conformers as an equilibrium mixture in solutions at room temperature. Differences in chemical shifts for α-hydrogen atoms of N-alkyl groups, as well as for H-2 in the imidazole ring are especially pronounced. Apparently, an influence of the anisotropic effect of the nitroso group on those hydrogen atoms should be the most significant.[5] In all *Z*-conformers, the α-hydrogen atom is shielded by 0.6-0.8 ppm in comparison with the corresponding signal for the *E*-conformer. For H-2 protons (or 2-CH_3 signal in **7d**), the situation is reversed, and the corresponding signal of the *E*-form appears at a lower field (by 0.4-0.6 ppm). Assignments to *E*- or *Z*-conformer were based on consideration of shielding and deshielding zones of magnetic cones of the nitroso group.[9]

Apparently, the *E/Z* izomeric ratio in solution depends upon two factors: steric effects, and the solvent polarity. Thus, with increasing size of N-alkyl group, the concentration of *E*-conformer decreases independently of solvent, and for the N-isopropyl derivative **7e** only the *Z*-form is observed in the ^{1}H NMR spectrum. Evidently, the *E*-izomer is sterically more hindered than the *Z*-form because of the close neighbourhood of the alkyl group and the oxygen atom.

Table 1. Bond lengths (l) and bond angles (θ) for compound **7d**.

Bond Lengths	l (Å)	Bond angles	θ (degree)
N(1)-C(7)	1.300(2)	C(7)-N(1)-C(6)	105.4(2)
N(1)-C(6)	1.405(3)	N(3)-N(2)-C(7)	124.81 (13)
N(2)-N(3)	1.380(2)	N(3)-N(2)-C(1)	125.30(13)
N(2)-C(7)	1.382(2)	C(7)-N(2)-C(1)	108.33(13)
N(2)-C(1)	1.389(2)	N(4)-N(3)-N(2)	119.9(2)
N(3)-N(4)	1.331(2)	N(4)-N(3)-C(9)	119.9(2)
N(3)-C(9)	1.449(3)	N(2)-N(3)-C(9)	120.1(2)
N(4)-O(1)	1.215(3)	O(1)-N94)-N(3)	115.(2)
C(1)-C(2)	1.389(3)	N(2)-C(1)-C(2)	132.1(2)
C(1)-C(6)	1.394(3)	N(2)-C(1)-C(6)	103.6(2)
C(2)-C(3)	1.384(3)	C(2)-C(1)-C(6)	124.3(2)
C(3)-C(4)	1.388(5)	C(3)-C(2)-C(1)	115.3(2)
C(4)-C(5)	1.384(4)	C(2)-C(3)-C(4)	122.0(2)
C(5)-C(6)	1.398(3)	C(5)-C(4)-C(3)	122.0(2)
C(7)-C(8)	1.487(3)	C(4)-C(5)-C(6)	117.5(2)
		C(1)-C(6)-C(5)	119.0(2)
		C(1)-C(6)-N(1)	110.8(2)
		C(5)-C(6)-N(1)	130.2(2)
		N(1)-C(7)-N(2)	111.7(2)
		N(1)-C(7)-C(8)	127.5(2)
		N(2)-C(7)-C(8)	120.8(2)

The influence of solvent polarity on the *E/Z* isomeric ratio is supported by the observation that the equlibrium is significantly shifted towards *Z*-isomer in DMSO in comparison with the chloroform solution. This can be explained by the higher polarity of the *Z*-form, and therefore by its better solvation in more polar solvents. Dipole moment vector of the benzimidazole molecule (μ ~ 4 D) is known to be approximately directed from the pyrrole to the pyridine nitrogen atom, [10] and that of the nitroso group is directed from the nitrogen to oxygen atom. Thus, in *Z*-form both dipole moment vectors should be added, whereas in *E*-form these should be subtracted. One can suggest that the dipole-dipole interactions also determine the existence of **7d** in the solid state as the *Z*-conformer.

To estimate the rotation energy barrier for the N-N(O) bond, the temperature dependent ^{1}H NMR spectra of **7a** were recorded (Figure 3). At elevated temperature, a classical picture of broadening and junction of both pairs of diagnostic signals, H-2 and α-hydrogen atoms of the N-alkyl group, was

observed, and at 120 °C their coalescence occured. Upon cooling all signals reappeared, and thus the assignments were confirmed as due to isomeric absorption. From a line-shape study of these coalescing doublets, it was possible to determine the values of free energy ($\Delta G^{\ddagger}$) and enthalpy ($\Delta H^{\ddagger}$) of activation for the rotation: $\Delta G^{\ddagger}$ = 75.5 kJ · mol $^{-1}$, $\Delta H^{\ddagger}$ = 67.5 kJ · mol $^{-1}$. The $\Delta G^{\ddagger}$ value is considerably lower than that for the N-nitroso derivatives of dimethylamine, azacycloalkanes, [5] or N-alkylanilines [6] where $\Delta G^{\ddagger}$ fell in a range of 90-110 kJ · mol $^{-1}$. Such a significant difference can be explained by a smaller contribution from bipolar structures **8a`** and **8b`** to a resonance hybrid of **7** due to a partial destabilization by the proximity of two positively charged nitrogen atoms – the pyrrole type heteroatom, and the nitrogen atom of the NNO group.

Table 2. Distribution of *E*- and *Z*-forms and diagnostic chemical shifts in ^{1}H NMR spectra for **7a-e**.

Compound	Solvent	*E*,*Z*, %	δ, ppm	
			H-2	α-Hydrogen atoms of N-alkyl group
7a	$CDCl_3$	E 60	8.12	3.58, CH_3
		Z 40	7.64	4.33, CH_3
	DMSO-d_6	E 47	8.74	3.65, CH_3
		Z 53	8.25	4.38, CH_3
7b	$CDCl_3$	E 33	8.07	4.10, CH_2
		Z 67	7.59	4.76, CH_2
	DMSO-d_6	E 25	8.76	4.16, CH_2
		Z 75	8.26	4.82, CH_2
7c	$CDCl_3$	E 40	7.62	5.17, CH_2
		Z 60	7.08	5.77, CH_2
	DMSO-d_6	E 24	8.50	5.34, CH_2
		Z 76	8.00	5.99, CH_2
7d	$CDCl_3$	E 52	2.50 *	3.53, CH_3
		Z 48	2.26 *	4.29, CH_3
	DMSO-d_6	E 42	2.49 *	3.64, CH_3
		Z 58	2.21 *	4.37, CH_3
7e	$CDCl_3$	Z 100	7.53	5.49, CH
	DMSO-d_6	Z 100	8.23	5.51, CH

* Signal of 2-CH_3 group.

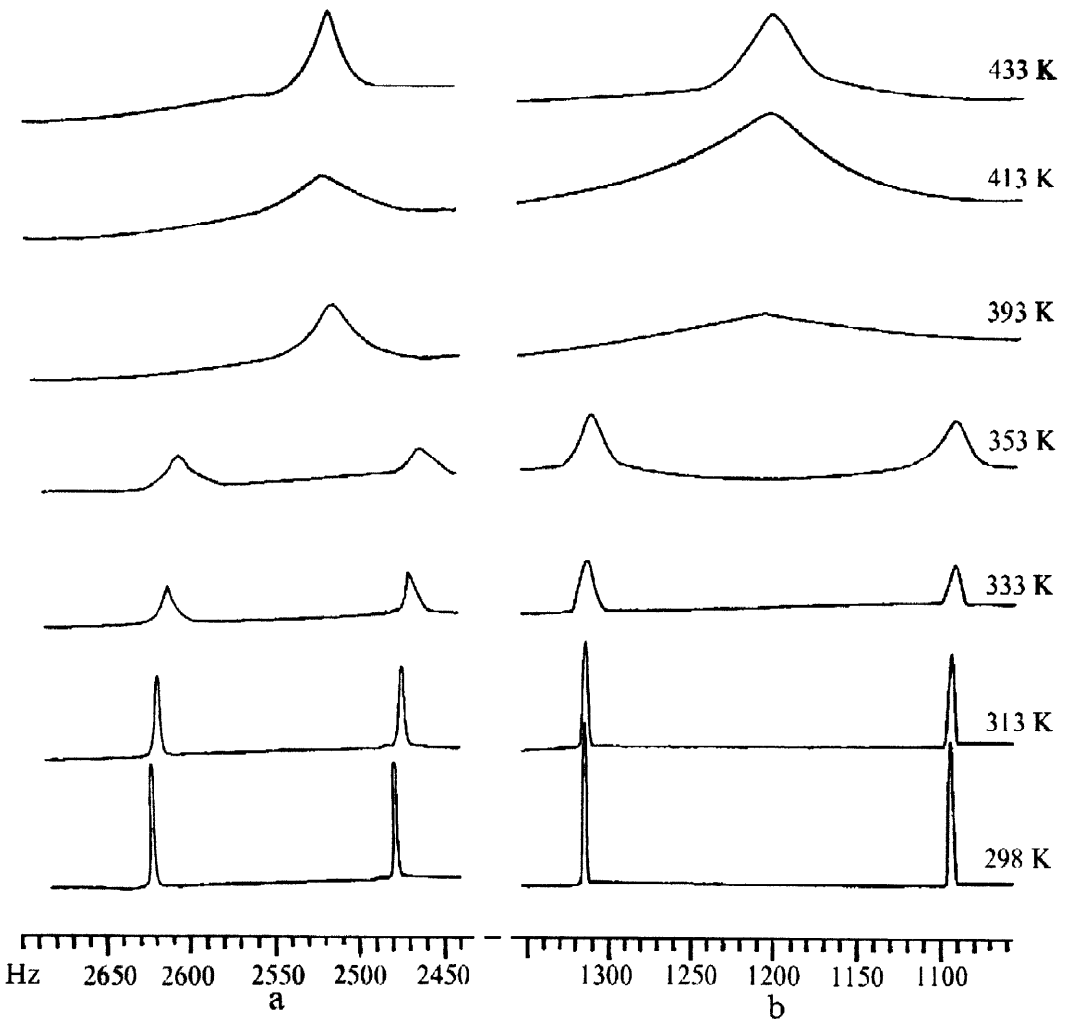


Figure 2. Temperature dependent ^{1}H NMR spectra of **7a** in DMSO-D_6: **a**- region of H-2 signal; **b** - region of N-metyl group.

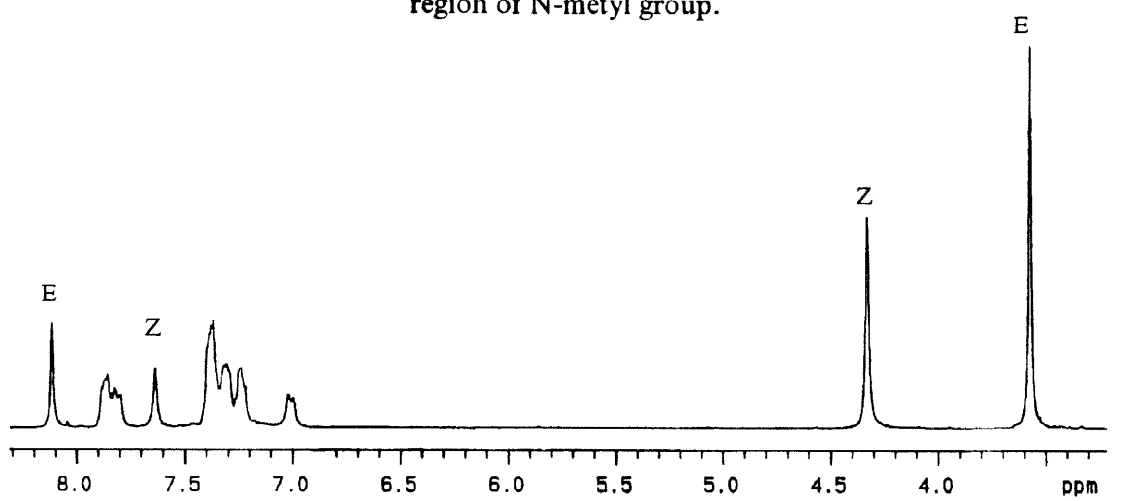
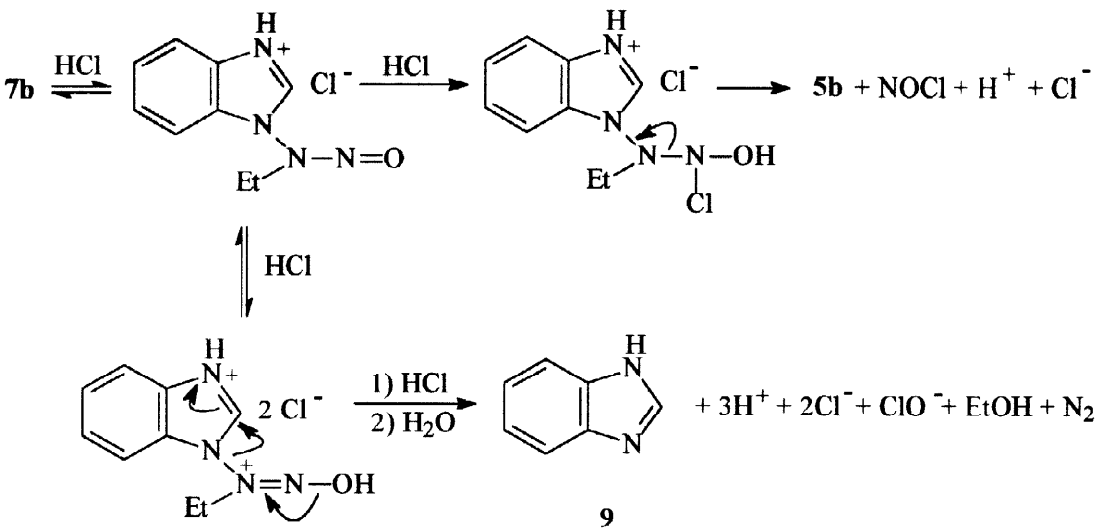


Figure 3. ^{1}H NMR spectrum of **7a** in $CDCl_3$.

Some Other Properties

Nitrosoamines **7** are readily hydrolyzed under acidic conditions. Thus, within 72 hours in concentrated hydrochloric acid at room temperature, the nitroso derivative **7b** was completely transformed into a mixture of 1-ethylaminobenzimidazole (**5b**) and benzimidazole (**9**) in 65 and 34 % yields, respectively. The reaction assumably proceeds as shown in Scheme **5**.

Scheme 5



Experimental

General. Melting points were determined in sealed glass capillaries and are uncorrected. ^{1}H NMR spectra were recorded on either a Unity-300 (300 MHz) or a Bruker-250 (250 MHz) spectrometer and chemical shifts are given in ppm downfield from $SiMe_4$. IR spectra were recorded using a UR-20 spectrometer (Germany). The EI-mass spectrum of **7a** was measured on a MX-1321A spectrometer. Al_2O_3 (II-III activity of Brockman) was used for chromatographic separations.

The starting 1-aminobenzimidazole derivatives were obtained in accordance with the following procedures: **2a**,[11] **2b**,[12] **3a**,[13] **5a-c**.[4]

X-Ray Structure Determination. Crystals of **7d** suitable for X-ray analysis were obtained by slow evaporation of the saturated ethanol solution. A colourless single crystal, 0.60 x 0.40 x 0.30 mm was chosen. Intensity data (2837 independent reflections) were collected at 293 K with graphite-monochromated Mo K_α radiation using a Siemens P3/PC diffractometer ($\theta/2\theta$ scan technique, θ_{max} = 30 °, no absorbtion correction was applied, μ (Mo-K_α) = 0.9 cm^{-1}). The structure was solved by a direct method and refined by a full-matrix least-squares procedure in anisotropic approximation for non-hydrogen atoms. All

hydrogen atoms were located in difference Fourier synthesis and included in the refinement with isotropical thermal parameters. Crystall data for $C_9H_{10}N_4O$, M = 190.21: monoclinic, $P2_1/n$, a = 6.930(2), b = 11.533(4), c = 12.359(4) Å , β = 101.68 (2) °, V = 967.3(6) ^{3} Å^3, D_{calc} = 1.306 g cm^3 for Z = 4. Final discrepancy factors are R1 = 0.0530 (on F for 2049 reflections with I > 2 σ(I)], wR2 = 0.1926 (on F^2 for all 2833 reflections used in the refinnement of 167 parameters). All calculations were carried out on an IBM PC with the help of SHELXTL PLUS 5 program.

Determination of Rotational Barriers by Coalescence Method. The rotational barrier was estimated based upon equation (1) where Δν is the chemical shift difference between the individual rotameric signals of methyl groups or 2-H protons and T_c is the temperature of coalescence.

$$\Delta G^{\ddagger} = 19.14\, T_c\, (9.97 + \log (T_c/\Delta\nu)) \quad kJ \cdot mol^{-1} \qquad (1)$$

Data: Δν = 220.91 Hz (N-Me), Δν = 145.39 Hz (2-H), T_c = 393 K.

1-Acetylamino-2-methylbenzimidazole (3b). A solution of 1.3 g (9 mmol) 1-amino-2-methylbenzimidazole in 300 ml glacial AcOH was heated at reflux for 5 h with simultaneous distillation of half volume of acid. The residue of acid was then evaporated and the crystals of **3b** were purified by crystallization from water. Yield 0.71 g (43 %). Colorless needles: mp 204-206 °C (water). Data: mp 206-208 °C. [13]

1-(Acetylmethylamino)-2-methylbenzimidazole (4d). A mixture of 0.71 g (3.8 mmol) 1-acetylamino-2-methylbenzimidazole (**3b**), 0.21 g (3.8 mmol) powdered KOH and 120 ml anhydrous acetone was stirred 10 min and 0.23 ml (3.8 mmol) methyl iodide was added. The solution was stirred for 4 h at room temperature. Solvent was distilled off and the residue was extracted with 15 ml $CHCl_3$. The chloroform solution was chromatographed on column with Al_2O_3 (l=20 cm, d=1.5 cm) using $CHCl_3$ as eluent. Yield 0.41 g (53 %). Colorless crystals: mp 102-103 °C (heptane). IR (nujol, ν, cm^{-1}): 3060, 1690, 1620, 1540. Anal. Calcd for $C_{11}H_{13}N_3O$: C, 65.01; H, 6.45; N, 20.67. Found: C, 65.13; H, 6.30; N, 20.62.

1-Methylamino-2-methylbenzimidazole (5d). A solution of **4b** (0.33 g, 1.5 mmol) in 20 ml 15 % HCl was refluxed for 2 h. After cooling and neutralization with conc. NH_4OH (pH 7-8), the mixture was extracted with $CHCl_3$ (3 x 15 ml). Evaporation of the solvent afforded 0.22 g (82 %) compound **5d**. Colorless crystals: mp 132-134 °C (heptane). IR (nujol, ν, cm^{-1}): 3230, 3080, 1560, 1510. ^{1}H NMR ($CDCl_3$, δ, ppm): 2.58 (c., 3H, C-CH_3); 2.94 (d, 3H, J=5.86 Hz, N-CH_3); 4.68 (q, 1H, J=5.57 Hz, NH), 7.22 (m, 2H, 5,6-H); 7.33 (m, 1H, 4-H); 7.65 (m, 1H, 7-H). Anal. Calcd for $C_9H_{11}N_3$: C, 67.06; H, 6.88; N, 26.07. Found: C, 66.89; H, 7.01; N, 25.97.

1-i-Propylaminobenzimidazole (5e). A solution of 0.67 g (5 mmol) **2a**, 0.9 ml (12 mmol) acetone and 2 drops conc. HCl in 20 ml i-PrOH was refluxed for 16 h. After evaporation of half volume of solvent 0.4 g (10 mmol) $NaBH_4$ was added at cooling. The suspension was kept at room temperature for 24 h. The resulting solution was poured into water (10 ml), acidified with conc. HCl to pH 6-7 and then

extracted with chloroform (3 x 15 ml). The $CHCl_3$ extracts were chromatographed on Al_2O_3 (l=20 cm, d=1.5 cm) using chloroform as eluent. In the first fraction (R_f 0.45) 0.33 g (37 %) compound **(5e)** was collected. Colourless leaflets: mp 100-101 °C (heptane). ^1H NMR ($CDCl_3$, δ, ppm): 1.11 (d, 6H, J=6.2 Hz, $(CH_3)_2$), 3.68 (m, 1H, CH), 4.90 (s, 1H, NH), 7.33 (m, 2H, 5,6-H), 7.46 (m, 1H, 4-H), 7.80 (m, 1H, 7-H), 7.98 (s, 1H, 2-H). Anal. Calcd for $C_{10}H_{13}N_3$: C, 68.54; H, 7.48; N, 23.98. Found: C, 68.77; H, 7.32; N, 24.17.

The second fraction (R_f 0.15) gave 0.22 g (33 %) of 1-aminobenzimidazole.

General procedure for the synthesis of 1-(N-nitrosoalkylamino)benzimidazoles (7a-e). To a solution of 2 mmol of the corresponding 1-(alkylamino)benzimidazole **(5a-e)** in 10 ml 35-% HCl cooling to -5 °C a solution of 2 mmol of $NaNO_2$ in water (3 ml) was added dropwise at a rate slow enough to maintain the temperature below 0 °C. A mixture was then kept at 0 °C 30 min and conc. NH_4OH was added to pH 7-8. The emulsion formed was extracted with $CHCl_3$ (3 x 5 ml) and the extract was chromatographed on a column with Al_2O_3 (eluent - $CHCl_3$). The fraction with R_f 0.6-0.75 was collected in each case affording compounds **(7a-e)**. With the exception of **7d** all other nitrosoaminoderivatives were studied without further purification.

1-(N-Nitrosomethylamino)benzimidazole (7a). Yield 57 %. IR (film, ν, cm^{-1}): 3080, 2970, 2930, 1630, 1510. ^1H NMR ($CDCl_3$, δ, ppm): 3.58 (s, 3H, CH_3, **E**), 4.33 (s, 3H, CH_3, **Z**), 7.02 (m, 1H, 4-H, **Z**), 7.24 (m, 1H, 4-H, **E**), 7.32-7.37 (m, 2H, 5,6-H, **E,Z**), 7.64 (s, 1H, 2-H, **Z**), 7.82 (m, 1H, 7-H, **Z**), 7.85 (m, 1H, 7-H, **E**), 8.12 (s, 1H, 2-H, **E**). ^1H NMR (DMSO-d_6, δ, ppm): 3.65 (s, 3H, CH_3, **E**), 4.38 (s, 3H, CH_3, **Z**), 7.30-7.57 (m, 3H, 4-6H, **E,Z**), 7.74 (m, 1H, 7-H, **Z**), 7.81 (m, 1H, 7-H, **E**), 8.25 (s, 1H, 2-H, **Z**), 8.74 (s, 1H, 2-H, **E**). ^{13}C NMR ($CDCl_3$, δ, ppm): 36.67 (^1J=43 Hz, CH_3, **Z**), 41.15 (^1J=141 Hz, CH_3, **E**), 108.65 (^1J=165.38 Hz, ^2J=7.58 Hz, ^3J=3.87 Hz, 4,7-C, **Z**), 121.24 (^1J=161.95 Hz, ^2J=7.8 Hz, ^3J=3.3 Hz, 4,7-C, **E**), 123.70 (5-C, **E**), 123.92 (^1J=159.95 Hz, 5-C, **Z**), 124.74 (^1J=158.7 Hz, 6-C, **E**), 125.06 (^1J=161.03 Hz, ^2J=7.2 Hz, 6-C, **Z**), 130.53 (4a,7a-C, **E**), 132.36 (4a,7a-C, **Z**), 140.24 (^1J=211.95 Hz, 2-C, **Z**), 140.78 (^1J=212.18 Hz, 2-C, **E**). Mass-spectra, m/z (I, %): 146 (100) (M^+-NO), 118 (20), 103 (18), 90 (16), 76 (22), 63 (10), 50 (19), 42 (30). Anal. Calcd for $C_8H_8N_4O$: C, 54.54; H, 4.58; N, 31.80. Found: C, 54.38; H, 4.40; N, 31.96.

1-(N-Nitrosoethylamino)benzimidazole (7b). Yield 62 %. IR (film, ν, cm^{-1}): 3080, 2980, 2940, 1620, 1500. ^1H NMR ($CDCl_3$, δ, ppm): 1.14 (t, 3H, J=7.25 Hz, CH_3, **E**), 1.49 (t, 3H, J=7.25 Hz, CH_3, **Z**), 4.10 (q, 2H, J=7.25 Hz, CH_2, **E**), 4.67 (q, 2H, J=7.18 Hz, CH_2, **Z**), 7.00 (m, 1H, 4-H, **Z**), 7.05 (m, 1H, 4-H, **E**), 7.30-7.36 (m, 2H, 5,6-H, **E,Z**), 7.59 (s, 1H, 2-H, **Z**), 7.81 (m, 1H, 7-H, **Z**), 7.85 (m, 1H, 7-H, **E**), 8.07 (s, 1H, 2-H, **E**). ^1H NMR (DMSO-d_6, δ, ppm): 1.04 (t, 3H, J=7.32 Hz, CH_3, **E**), 1.40 (t, 3H, J=7.17 Hz, CH_3, **Z**), 4.16 (q, 2H, J=7.25 Hz, CH_2, **E**), 4.82 (q, 2H, J=7.17 Hz, CH_2, **Z**), 7.29-7.39 (m, 2H, 5,6-H, **E,Z**), 7.53 (m, 1H, 4-H, **Z**), 7.56 (m, 1H, 4-H, **E**), 7.74 (m, 1H, 7-H, **Z**), 7.81 (m, 1H, 7-H, **E**), 8.26 (s, 1H, 2-H, **Z**), 8.76 (s, 1H, 2-H, **E**). Anal. Calcd for $C_9H_{10}N_4O$: C, 56.83; H, 5.30; N, 29.46. Found: C,

56.68; H, 5.45; N, 29.42.

1-(N-Nitrosobenzylamino)benzimidazole (7c). Yield 53 %. IR (film, ν, cm^{-1}): 3080, 2980, 2935, 1590, 1480. ^1H NMR ($CDCl_3$, δ, ppm): 5.17 (s, 2H, CH_2, **E**), 5.77 (s, 2H, CH_2, **Z**), 6.78 (m, 1H, 4-H, **Z**), 7.02 (m, 1H, 4-H, **E**), 7.08 (s, 1H, 2-H, **Z**), 7.14-7.42 (m, 2H, 5,6-H, **E,Z**), 7.62 (s, 1H, 2-H, **E**), 7.75 (m, 1H, 7-H, **Z**), 7.81 (m, 1H, 7-H, **E**). ^1H NMR (DMSO-d_6, δ, ppm): 5.34 (s, 2H, CH_2, **E**), 5.99 (s, 2H, CH_2, **Z**), 6.78 (m, 1H, 4-H, **Z**), 7.11 (m, 1H, 4-H, **E**), 7.12-7.45 (m, 2H, 5,6-H, **E,Z**), 7.64 (m, 1H, 7-H, **Z**), 7.69 (m, 1H, 7-H, **E**), 8.00 (s, 1H, 2-H, **Z**), 8.05 (s, 1H, 2-H, **E**), Anal. Calcd for $C_{14}H_{12}N_4O$: C, 66.65; H, 4.79; N, 22.21. Found: C, 66.46; H, 4.73; N, 22.39.

1-(N-Nitrosomethylamino)-2-methylbenzimidazole (7d). Yield 69 %, m.p. 76-78 °C (heptane). IR (nujol, ν, cm^{-1}): 1620, 1550, 1490. ^1H NMR ($CDCl_3$, δ, ppm): 2.26 (s, 3H, C-CH_3, **Z**), 2.50 (s, 3H, C-CH_3, **E**), 3.53 (s, 3H, N-CH_3, **E**), 4.29 (s, 3H, N-CH_3, **Z**), 6.92 (m, 1H, 4-H, **Z**), 7.10 (m, 1H, 4-H, **E**), 7.16-7.37 (m, 2H, 5,6-H, **E,Z**), 7.67 (m, 1H, 7-H, **Z**), 7.74 (m, 1H, 7-H, **E**). ^1H NMR (DMSO-d_6, δ, ppm): 2.21 (s, 3H, C-CH_3, **Z**), 2.49 (s, 3H, C-CH_3, **E**), 3.64 (s, 3H, N-CH_3, **E**), 4.37 (s, 3H, N-CH_3, **Z**), 7.20-7.28 (m, 2H, 5,6-H, **E,Z**), 7.30 (m, 1H, 4-H, **Z**), 7.41 (m, 1H, 4-H, **E**), 7.60 (m, 1H, 7-H, **Z**), 7.68 (m, 1H, 7-H, **E**). Anal. Calcd for $C_9H_{10}N_4O$: C, 56.83; H, 5.30; N, 29.46. Found: C, 57.03; H, 5.37; N, 29.72.

1-(N-Nitroso-i-propylamino)benzimidazole (7e). Yield 60 %. IR (film, ν, cm^{-1}): 3080, 2980, 2930, 1680, 1480. ^1H NMR ($CDCl_3$, δ, ppm): 1.57 (s, 6H, $(CH_3)_2$), 5.49 (septet, 1H, J=6.7 Hz, CH), 7.02 (m, 1H, 4-H), 7.27-7.36 (m, 2H, 5,6-H), 7.53 (s, 1H, 2-H), 7.83 (m, 1H, 7-H). ^1H NMR (DMSO-d_6, δ, ppm): 1.54 (d, 6H, J=5.93 Hz, $(CH_3)_2$), 5.51 (septet, 1H, J=6.62 Hz, CH), 7.25-7.37 (m, 3H, 4-6-H), 7.77 (m, 1H, 7-H), 8.23 (s, 1H, 2-H). Anal. Calcd for $C_{10}H_{12}N_4O$: C, 58.81; H, 5.92; N, 27.43. Found: C, 58.67; H, 6.01; N, 27.55.

Denitrosation of 1-(N-nitrosoethylamino)benzimidazole (7b). A solution of **7b** (0.38 g, 2 mmol) in 10 ml conc. HCl was kept for 72 h at room temperature. The mixture was neutralized with conc. NH_4OH to pH 7-8 and extracted with $CHCl_3$ (3x5 ml). The extract was evaporated for small volume and was chromatographed on alumina (d=1.5 cm, l=20 cm), using $CHCl_3$ as eluent. In the first fraction (R_f 0.4) 0.21 g (65 %) compound **5b** (mp 100-101 °C (heptane)) was collected. Using then as eluent 3:1 $CHCl_3$ – EtOH fraction with R_f 0,1 containing compound (**9**) was collected. Yield 0.08 g (34 %).

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