# SPECIAL FEATURES OF THE STERIC
AND ELECTRONIC STRUCTURE OF
BIS(3-IMINO-1-ISOINDOLINYLIDENEAMINO)-
ARYLENES ACCORDING TO
DATA OF THE AM1 METHOD

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Using the semiempirical AM1 method stationary points have been found on the potential energy surfaces for the internal rotation of 1,3-bis(3-imino-1-isoindolinylideneamino)benzene and 2,6-bis(3-imino-1-isoindolinylideneamino)pyridine, and also for their tautomeric forms. Energy barriers for the in-plane inversion of the terminal imino groups and for the tautomeric conversions involving them have been determined. It was shown that the molecules of these compounds are structurally flexible.

Keywords: bis(3-imino-1-isoindolinylideneamino)arylenes, AM1 calculations, internal rotation, inversion of imino groups, tautomerism.

Bis(3-imino-1-isoindolinylideneamino)arylenes **1, 2** are important intermediates in the synthesis of macroheterocyclic compounds [1-3]. However in spite of their similarity in structure these compounds display different reactivities. Compound **1** on interaction with 1,3-diiminoisoindoline forms a macrocyclic system containing three isoindolin-1,3-diylidene residues and one *meta*-phenylene fragment, while no analogous product is obtained from compound **2** under these conditions [2,3].
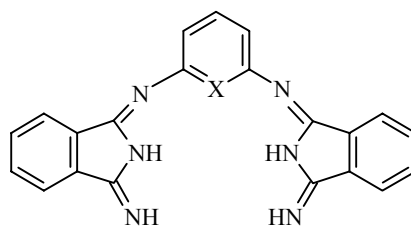
1 X = CH; **2** X = N

A structural feature of the three-ring products **1** and **2** is the presence of two fairly substantial isoindoline fragments combined with a residue of diamine by aza bridges. This probably determines the inclination of the molecules to form nonplanar structures as a result of internal rotation relative to the single N–C

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bond. In addition, by analogy with 1,3-diiminoisoindoline [4], it would be expected that similar compounds may display an inclination towards in-plane inversion of the terminal imino groups and also towards tautomeric conversions. These special features of the structure, determining to a significant extent the reactivity of products **1** and **2** in reactions with both diamines and with 1,3-diiminoisoindoline, have been inadequately studied up to the present. Consequently the aim of the present work was to study theoretically the special features of the spatial and electronic structures for compounds **1** and **2** with the aid of the AM1 quantum-chemical method [5]. The calculations were carried out using the MOPAC-93 program package [6] on a CONVEX C3220 computer in the Cracow Calculation Center CYFRONET.

In particular, the energy profiles for internal rotation of the isoindole fragment around the single $C_{(6)}$–$N_{(1)}$ bond in **1** and **2** were studied, and also for the isoindolenine and isoindole fragments around the $C_{(6)}$–$N_{(1)}$ and $C_{(2)}$–$N_{(2)}$ bonds for their amino-imino forms **1a** and **2a** (Table 1). The size of the dihedral angle $C_{(5)}$–$C_{(6)}$–$N_{(1)}$–$C_{(7)}$ (for all compounds) or $C_{(3)}$–$C_{(2)}$–$N_{(2)}$–$C_{(8)}$ (for tautomers **1a** and **2a**) was varied from 0 to 360° with a step of 10°. A complete optimization was carried out for each point for all the remaining parameters. The positions of the stationary points on the potential energy surface were refined with the aid of the EF, NLLSQ, and TS procedures [6], after which the points were verified to conform with the critical condition [6,7].

Three hydrogen atoms are disposed in the "internal sphere" of 1,3-bis(3-imino-1-isoindolinylideneamino)benzene (**1**), two atoms are of the cyclic imino groups of the isoindole fragments and one hydrogen atom of the benzene ring. In the case of the planar structure **A0** (Table 1), assigned to the symmetry point group C_{2v}, these atoms are close in space as a result of which a significant repulsion is observed between them, which is displayed, in particular, in an increase of the valence angle at the bridge nitrogen atoms to 129.9°. From the data given in Table 1 and in Fig. 1a four minima are detected in the configurational space investigated in the case of compound **1**, which correspond to rotamers **A**, **C**, **E**, and **G**. The indole nuclei in structures **A** and **C** are disposed on different sides of the plane of the central benzene nucleus, which enables them to be called *E* isomers, while **E** and **G** are *Z* isomers (Fig. 2*a,b*).

The rotary isomers **A** and **C**, and also **E** and **G** are separated by the low energy barriers **B** and **F** respectively, not exceeding 0.7 kcal/mole, which indicates a high rate of exchange between them. The rate constant (*k*), calculated from the data of [8] for 298 K and $\Delta\Delta G = 0.76$ kcal/mole, is approximately 10^{12} sec^{-1}. The appearance of these barriers at values of φ close to 90 and 270° may indicate the presence of conjugation between the isoindole and benzene fragments.

Transition between the *E*- and *Z*-conformers (**C-D-E**), and also internal rotation through the transition state **H** is also effected with low activation barriers not exceeding 3.5 kcal/mole ($k \sim 10^{10}$ sec^{-1}). The given molecule may be referred to as being structurally flexible with restrained internal rotation and a marked inclination towards rotary isomerism.

Only two hydrogen atoms of the cyclic imino groups are present in the internal cavity of compound **2**, which leads to a reduction of the repulsion between them compared with compound **1**. In particular, the valence angle at the bridge nitrogen atom for the planar configuration **A0** of compound **2** (Table 1) is less than in the case of structure **A0** for compound **1**.

The potential energy surface cross section for the internal rotation of compound **2** (Fig. 1b) proved to be symmetrical relative to φ = 180°, and structures **A** and **C** are mirror isomers. The transition between them, characterized by an activation barrier of 0.25 kcal/mole and indicating a rapid conformational exchange ($k \sim 10^{12}$ sec^{-1}), and also the value of the barrier to internal rotation (10.14 kcal/mole, $k \sim 10^{5}$ sec^{-1}), localized at φ close to 0°, indicate that this molecule may also be referred to as being structurally flexible with internal rotation. The reason for the large restraint in this case is probably stabilization of structures **A** and **C** as a result of forming an intramolecular hydrogen bond between the hydrogen atoms of the cyclic imino groups and the nitrogen atom of the pyridine ring.

In the case of the low symmetry amino-imino derivatives **1a** and **2a**, energy profiles were studied for internal rotation of the isoindolenine fragments **1a** (**A-H**), **2a** (**A-D**) and the isoindole fragments **1a** (**I-P**), **2a** (**E,F**) (Table 1, Figs. 1,2).
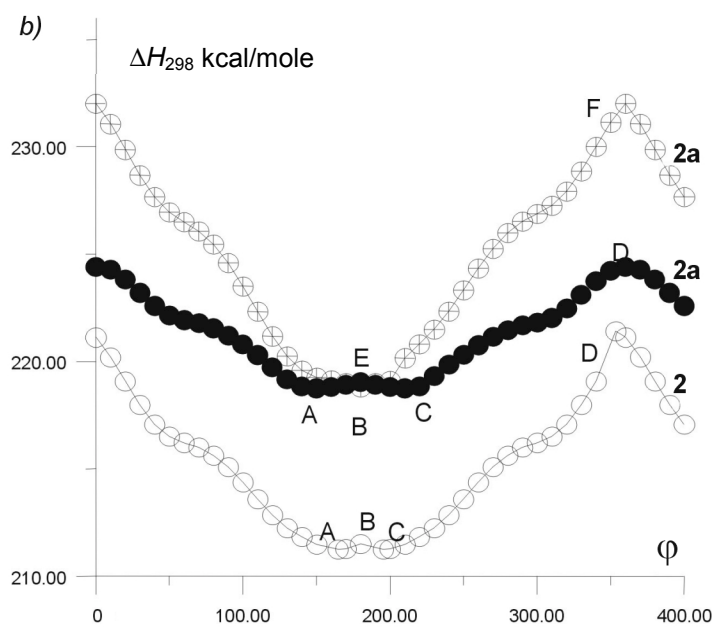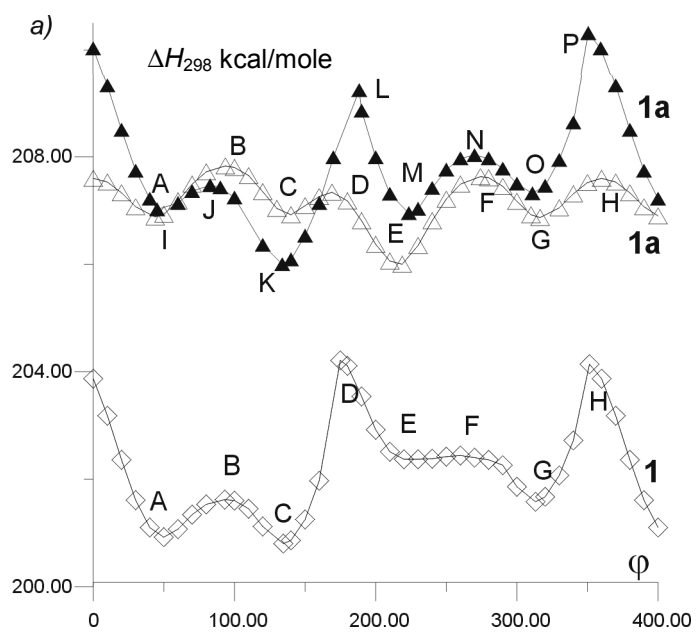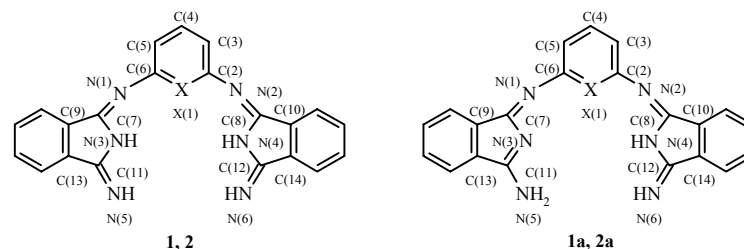
Fig. 1. Profiles of the potential energy surface for the internal rotation of
bis(1-imino-3-isoindolylideneamino)arylenes **1, 2** and their tautomeric forms **1a, 2a**.

TABLE 1. Basic molecular properties of the rotamers of bis(1-imino-3-isoindolylideneamino)arylenes **1** and **2** and their tautomeric forms **1a** and **2a**

1, 2   **1a, 2a**

Com-pound	Rotamer*	Angle (deg.)				Distance $N_{(5)}$–$N_{(6)}$ [Å]	Dipole moment [D]	Charge on atom × 10³ (charge units)				ΔH_{298} [kcal/mole]*²	ΔS_{298} [cal/mole·K]	ΔG_{298} [kcal/mole]
		$C_{(5)}$–$C_{(6)}$–$N_{(1)}$–$C_{(7)}$	$C_{(3)}$–$C_{(2)}$–$N_{(2)}$–$C_{(8)}$	$C_{(6)}$–$N_{(1)}$–$C_{(7)}$	$C_{(2)}$–$N_{(2)}$–$C_{(8)}$			$N_{(5)}$	$C_{(11)}$	$N_{(6)}$	$C_{(12)}$			
1	2	3	4	5	6	7	8	9	10	11	12	13	14	15
1 (X = CH)	**A0**	180.0	180.0	129.9	129.9	5.59	1.88	-253	136	-253	153	207.98	126.1	170.40
	A	49.9	136.0	122.8	123.0	11.54	0.31	-260	148	-263	154	200.92	122.9	164.30
	B	93.1	135.0	122.3	1.22.9	10.38	0.39	-262	152	-262	152	201.62	122.7	165.06
	C	134.6	134.6	122.9	122.9	8.54	0.75	-261	151	-261	151	200.80	120.5	164.89
	D	175.9	132.9	130.6	122.7	6.80	1.62	-260	149	-256	138	204.21	122.6	167.67
	E	233.4	140.9	122.6	124.2	5.67	1.46	-256	139	-264	158	202.36	123.1	165.68
	F	258.0	139.2	122.5	123.7	6.85	1.42	-257	140	-264	155	202.44	122.9	165.82
	G	313.2	137.7	123.3	123.4	9.66	1.27	-262	151	-263	153	201.58	122.9	164.96
	H	351.4	136.7	129.9	123.1	11.11	0.66	-257	141	-263	154	204.14	123.9	167.22
2 (X = N)	**A0**	180.0	180.0	126.2	126.2	4.37	1.38	-256	139	-256	139	212.62	123.9	175.70
	A	164.7	164.7	125.2	125.2	4.94	1.19	-261	149	-261	149	211.25	123.3	174.51
	B	180.0	204.5	125.7	124.6	4.81	1.25	-258	144	-261	149	211.50	123.5	174.70
	C	195.3	195.3	125.2	125.2	4.94	1.19	-261	149	-261	149	211.25	123.3	174.51
	D	353.3	179.5	129.4	125.4	11.00	1.51	-254	143	-265	158	221.41	125.5	184.01

TABLE 1 (continued)

1	2	3	4	5	6	7	8	9	10	11	12	13	14	15
1a	**A0**	180.0	180.0	127.9	129.7	5.16	3.81	-335	167	-267	148	209.87	123.9	172.95
(X = CH)	**A**	43.7	136.5	124.1	123.0	11.57	4.82	-342	168	-267	154	206.88	123.3	170.14
	B	93.5	136.5	123.0	123.0	10.31	4.65	-340	166	-267	153	207.83	123.0	171.18
	C	140.0	136.5	124.1	123.1	7.98	4.05	-337	165	-268	154	206.92	122.4	170.44
	D	169.0	134.7	127.3	123.1	6.42	4.63	-337	168	-270	158	207.34	122.5	170.84
	E	215.8	133.8	124.0	121.6	4.61	4.58	-340	171	-279	165	206.00	122.5	169.50
	F	274.2	135.1	123.0	122.7	7.54	5.00	-343	168	-268	153	207.63	122.7	171.07
	G	316.5	136.3	124.0	123.0	9.85	4.98	-338	164	-266	152	206.87	122.8	170.28
	H	360.0	136.7	127.4	123.1	11.29	4.66	-340	169	-267	153	207.60	126.1	170.02
	I	220.6	50.7	123.9	122.7	9.43	5.14	-337	164	-264	147	207.02	126.1	169.44
	J	220.3	82.7	123.9	122.1	7.64	5.10	-337	165	-226	148	207.47	122.9	170.85
	K	215.7	133.8	124.0	121.6	4.61	4.60	-341	172	-279	164	206.00	122.5	169.50
	L	215.3	188.4	124.7	130.1	6.18	4.90	-334	162	-264	144	209.22	122.8	172.63
	M	220.7	223.5	124.1	123.1	8.15	3.99	-339	167	267	152	206.95	123.0	170.30
	N	220.1	270.0	124.2	122.2	10.30	5.01	-340	166	-266	153	208.03	123.5	171.23
	O	220.9	311.0	124.1	122.8	11.49	4.93	-338	165	-264	148	207.32	123.4	170.55
	P	221.1	351.3	124.0	130.0	11.32	4.93	-332	164	-261	141	210.31	123.3	173.57
2a	**A0**	180.0	180.0	127.9	129.7	5.16	3.69	-335	167	-267	148	219.22	126.9	181.40
(X = N)	**A**	149.9	187.5	124.5	125.1	4.45	4.22	-335	159	-275	160	218.76	121.3	182.61
	B	180.0	191.6	126.5	124.8	4.11	3.76	-336	162	-278	159	219.05	124.7	181.89
	C	210.0	172.2	124.5	125.1	4.44	4.22	-335	159	-275	160	218.76	121.6	182.52
	D	360.8	180.2	126.4	125.4	11.05	5.49	-334	180	-270	159	224.42	125.0	187.17
	E	150.0	187.6	124.5	125.1	4.45	4.22	-335	167	-267	148	219.20	126.9	181.38
	F	352.6	227.8	12.6	129.6	11.25	4.08	-331	158	-258	141	232.35	123.6	195.52
3	—	134.5	222.3	122.8	123.0	5.04	5.44	-278	159	-268	148	155.42	140.5	113.55
3a	—	125.9	226.3	121.9	122.5	5.09	5.99	-357	188	-358	186	127.14	143.9	84.26
4	—	180.2	191.3	122.7	122.0	3.57	3.89	-253	153	-250	144	91.27	137.8	50.21

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* Rotamers **A0** are not found on the free rotation route of compounds **1**, **2** and **1a**, **2a**.
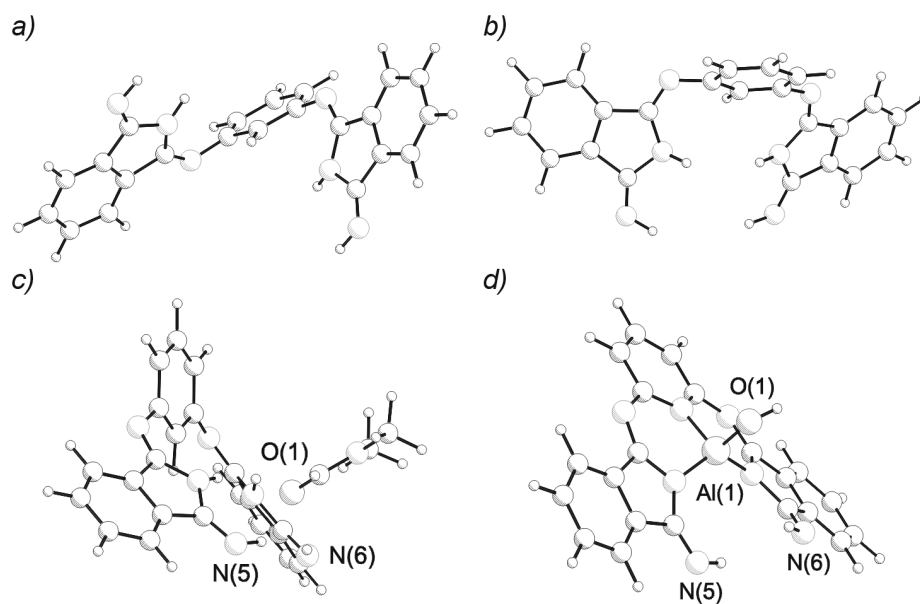
*[2] 1 kcal = 4.18 kJ.

Fig. 2. PLUTO models for rotamers *a*) **C** and *b*) **E** of bis(1-imino-3-isoindolylideneamino)benzene **1**, *c*) solvate **3**, and *d*) the complex with aluminum **4**.

On the whole the character of the energy profiles was retained on transition from molecules **1** and **2** to their tautomers **1a** and **2a** respectively (Table 1, Fig. 1*a,b*). The lower values of the activation barriers for rotation of fragments with a primary amino group is explained by the absence of hydrogen at atom $N_{(3)}$. The molecules **1a** and **2a** may therefore also be referred to as having a flexible structure with restraint of internal rotation and a marked inclination towards rotary isomerism. We note that the enthalpy of formation of the isomers as a result of internal rotation, in-plane inversion, and tautomerism is changed insignificantly, as a result of which the Gibbs free energy changes in agreement with the entropy (Table 1).

The structural flexibility of compounds **1** and **2** may be caused by in-plane inversion of the terminal imino groups [9]. With this aim the possibility of forming topomers at one of the terminal imino groups in compounds **1** and **2** for the *E*- and *Z*-configuration was studied. The calculated data are given in Table 2.

It was established that the corresponding stable *trans* isomers are formed as a result of the in-plane inversion. The activation barriers for the transitions between them are at the level of 22 kcal/mole ($k \sim 10^{-3}$ sec^{-1}) which also serves as a basis for referring to these molecules as structurally flexible. We note that these characteristics are in good agreement with the results obtained for 1,3-diiminoisoindoline (22.13 kcal/mole) [4], and also with the experimental values of the barriers for in-plane inversion of N-alkyl- and N-arylketimines (10-40 kcal/mole) [10,11].

The tautomeric conversions may introduce a contribution to the structural flexibility of the molecules [10]. It follows from the data of Table 2 that an activation energy of the order of 75 kcal/mole is required to carry out the tautomeric conversions **1** → **1a** and **2** → **2a** by an intramolecular mechanism in the gas phase. This is in good agreement with the analogous characteristic calculated by the AM1 method in the case of 1,3-diiminoisoindoline [4], and also by the *ab initio* method (basic 4-31G) for formamidine [12]. The rotamers **C** and **E** of compound **1** and rotamer **A** of compound **2** differ from the corresponding tautomeric structures of compounds **1a** and **2a** by a fairly high energy barrier and intramolecular transitions over the barrier do not introduce a significant contribution to the structural flexibility of the molecules being considered.

TABLE 2. Basic Thermodynamic Characteristics of the In-Plane Inversion (direction a) and Tautomeric Conversions (direction b) of Bis(1-imino-3-isoindolylideneamino)arylenes **1** and **2**

trans-[**1(C)**, **1(E)**, **2(A)**] **1(C)**, **1(E)**, **2(A)** **1a(C)**, **1a(E)**, **2a(A)**
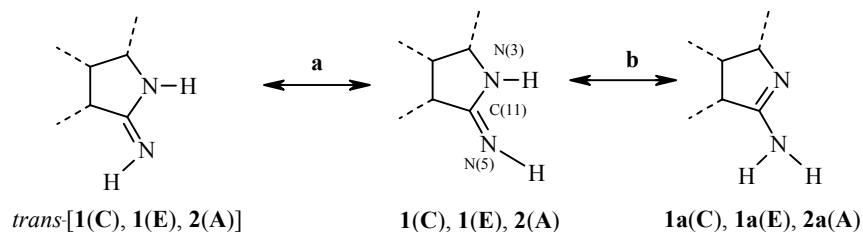
Direction	Transition	ΔH^{o}_{298} [kcal/mole]	ΔG^{o}_{298} [ксal/mole]
a	**1(C)** $\rightarrow$ trans-**1(C)**	22.22	21.31
	1(E) $\rightarrow$ trans -**1(E)**	21.65	21.72
	2(A) $\rightarrow$ trans -**2(A)**	22.05	21.59
b	**1(C)** $\rightarrow$ **1a(C)**	75.87	75.31
	1(E) $\rightarrow$ **1a(E)**	74.66	74.91
	2(A) $\rightarrow$ **2a(A)**	76.60	76.01

In view of the fact that the spatial structure of flexible molecules depends to a significant degree on external factors, the preferred content of one or another form in solution may be determined by the nature of the solvent [13,14]. With the aim of assessing the influence of an aprotic solvent, calculations were carried out on compound **3,** a solvate of compound **1** with a molecule of DMF (Table 1, Fig. 2, c).

The solvate **3** is formed by intermolecular hydrogen bonds between the imino group hydrogen atoms and the unshared electron pairs of the oxygen atom of the solvent. The molecule of the three-unit product is in this case in the Z-configuration. Forming the given structure is energetically advantageous since its enthalpy of formation is about 11 kcal/mole less than the sum of the enthalpies of formation of structure **A** and DMF, which in turn is significantly greater than the value of the barriers for internal rotation. A similar structure (**3a**, Table 1) is obtained by calculations on molecule **3** surrounded by a solvated sheath of DMF (AM1/COSMO program, EPS = 36.7, NSPA = 42 [6,15]). It turned out that the molecule of the three-unit product retains the Z-configuration, but the contribution of the DMF molecule was about 30% of the calculated solvation energy, equal to 39.46 kcal/mole. By specific solvation the solvent therefore gives rise to a displacement of the conformational equilibrium in the direction of forming a stable solvate.

The reactivity of the terminal imino groups is of particular interest from the point of view of synthesizing macroheterocyclic compounds. It follows from the data given in Table 1 that the presence of a benzene or pyridine nucleus and also the spatial disposition of the isoindole fragments do not show a significant influence on the charge distribution at these groups. The charges on the $N_{(5)}$ nitrogen atom for the E-configurations of **1** and **2** are the same, and the charges on the $C_{(5)}$ atoms differ insignificantly. Consequently the differences mentioned above in the reactivity of these compounds may not be explained by the differences in charge on these groups. Seemingly this may be linked with disturbance of the geometric correspondence between the reaction centers in the products of 1,3-diiminoisoindoline addition to compound **2**.

Similar structures of the chelate type may be stabilized by complex formation [1,16]. The effect of complex formation on the special features of spatial and electronic structure has been considered for the complex of compound **2** with aluminum (structure **4**) containing a hydroxyl group as axial ligand (Table 1, Fig. 2, d).

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The calculated data showed that the ligand molecule was rigidly fixed in the *Z*-configuration. In this case the charges on the nitrogen and carbon atoms of the terminal imino groups are changed only insignificantly compared with the analogous characteristics for structure **2** (**A**). In addition, the distance between the nitrogen atoms under consideration was reduced to 3.57 Å, which explains the attraction of this structure for template condensation. This conclusion is in agreement with experimental data. In particular in [16] the corresponding complex of an unsymmetrical pyridine macroheterocyclic compound was obtained by template condensation of complex **4** with 1,3-diiminoisoindoline in phenol.

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