Synthesis, structure, and dynamic behavior in solution of arylamino-1,3,5-triazines 1. Unsymmetrically substituted arylamino-1,3,5-triazines

P. A. Belyakov,^a* A. V. Shastin,^b and Yu. A. Strelenko^a

 ^aN. D. Zelinsky Institute of Organic Chemistry, Russian Academy of Sciences, 47 Leninsky prosp., 119991 Moscow, Russian Federation. E-mail: pbel@server.ioc.ac.ru
^bInstitute of Problems of Chemical Physics, Russian Academy of Sciences, 1 prosp. Akad. Semenova, 142432 Chernogolovka, Moscow Region, Russian Federation. Fax: +7 (496) 515 3588. E-mail: shastin@icp.ac.ru

Ten unsymmetrically substituted arylamino-1,3,5-triazines were synthesized and studied by dynamic NMR spectroscopy. The free energies of the hindered rotation ΔG^{\neq} are in 59—77 kJ mol⁻¹ range. Using difference-mode NOE NMR experiments, the structures of the major and minor rotation isomers were proved. The DFT B3LYP/6-31G* calculations were performed. The difference between the calculated rotation barriers and the experimental values obtained by line shape analysis is less than 7.6 kJ mol⁻¹. The height of the rotation barrier varies in a 18 kJ mol⁻¹ range depending on the substituents in the triazine ring.

Key words: arylamino-1,3,5-triazines, synthesis, structure in solution, hindered rotation, activation parameters, substitution effects, dynamic NMR spectroscopy, DFT B3LYP/6-31G* calculations.

The internal dynamics of organic compounds has a pronounced influence on their thermodynamic, electrical, optical, chemical, and other properties, which is especially important for biochemical processes, for understanding of the mechanisms of action, and for the design of new biologically active substances, first of all, medical drugs.¹

1,3,5-Triazines, or *symm*-triazines, have been known² for more than 100 years. Their derivatives are used as herbicides, pesticides,^{3,4} drugs,⁵ as the base for the liquid-phase or carrier-supported combinatorial libraries,⁶ and as condensing reagents in peptide synthesis.⁷ Recently, a fully unsymmetrically substituted triazine has been found in the algae *Halimeda xishaensis*, isolated, and characterized by a set of physicochemical methods.⁸ This was the first aromatic *symm*-triazine found in a natural object (for discussion on this point, see Ref. 9).

The hindered rotation in substituted 1,3,5-triazines has been discovered not long ago; therefore, data on the stereodynamics of these compounds are few^{10–15} as compared with the data on the synthesis and other properties of 1,3,5-triazines, which were considered in more than a thousand publications during the last 5 years alone. Initially, it was found that the NMR spectra of symmetrically substituted alkyl(aryl)amino-1,3,5-triazines exhibit double sets of signals for the substituents in the triazine ring.¹⁰ At higher temperatures, only one set of signals remains. The discovered process cannot be attributed to inversion of the nitrogen lone pair or to prototropic tautomerism. The presence of electron-withdrawing substituents in the triazine ring and different substituents at the exocyclic nitrogen atom are necessary conditions for observing two or several conformational isomers of amino-1,3,5-triazines in the NMR spectra at room temperature.¹⁶ For diamino-1,3,5-triazines, the coalescence temperature is usually <0 °C and for triamino-1,3,5-triazines, it is close to the freezing point of the solvent.¹¹ For a number of amino-1,3,5-triazines, the activation energies have been determined and the rotation barriers have been calculated theoretically.¹¹⁻¹⁵ The researchers cited attribute the hindered rotation in substituted amino-1,3,5triazines to the electron-withdrawing properties of the triazine ring, resulting in a higher C_{tr}-N_{am} bond order (tr is triazine, am is amine). Earlier studies into the dynamic effects are represented by scattered examples. The free activation energies of hindered rotation determined in these studies for various compounds using the Winn-Jones equation¹⁷ cannot be properly compared with one another, as these values have been obtained for different temperatures (at the coalescence points). No data are available on the stereodynamics of substituted arylamino-1,3,5-triazines, which are of obvious theoretical

Published in Russian in Izvestiya Akademii Nauk. Seriya Khimicheskaya, No. 10, pp. 2366-2376, October, 2005.

1066-5285/05/5410-2441 © 2005 Springer Science+Business Media, Inc.

interest from the standpoint of interaction of two classical aromatic¹⁸ systems. The activation parameters for the rotation about the C_{tr}-N_{Ar} bond in the arylamino-substituted *symm*-triazines have not been found in the literature either. In addition, the hindered rotation in unsymmetrically substituted triazines has been scarcely studied and no data on the ΔH^{\neq} or ΔS^{\neq} values in the fully unsymmetrically substituted *symm*-triazines are available. Meanwhile, 1,3,5-triazines are excellent model compounds for investigating hindered rotation in the heterocyclic series.

Study of the hindered rotation processes has also a practical value as regards the study of biological objects. In particular, in the case of 1,3,5-triazines, dynamic NMR was used to estimate the efficiency of drugs employed for decreasing the multidrug resistance of tumor cells.¹⁴

In a study of hindered rotation in unsymmetrically substituted 2-chloro-4-methoxy-6-phenylamino-1,3,5triazine (1), we found that the sterically more hindered rotation isomer is thermodynamically more stable in solution.¹⁹ Here we continued the study of this phenomenon in the series of unsymmetrically and symmetrically substituted analogs of compound 1 using quantum chemical calculations and dynamic NMR. The purpose of this study was to gain information on the activation parameters of the hindered rotation in arylamino-1,3,5-triazines with various substituents and to analyze the effect of the substituent nature in the triazine ring and the steric effect of the arylamine group on the height of the barrier to hindered rotation. Dynamic NMR line shape analysis (LSA) for arylamino-1,3,5-triazines has been carried out.²⁰ LSA is the most accurate method for determining the rate constants for two-position exchange.21,22

The study was carried out with alkoxy- and perfluoroalkoxy-substituted anilinochlorotriazines 2-10, symmetric and unsymmetric analogs of compound 1. They were chosen from the following considerations: in monoarylamino-substituted alkoxytriazines, only one bond is involved in the hindered rotation; variation of the substituents in the triazine ring allows one to change its electronwithdrawing properties; the introduction of various substituents into the arylamine fragment provides the possibility of estimating the substituent contributions. The use of perfluoroalkoxy groups pursued two goals, namely, the change in the donor-acceptor properties of the substituents and an increase in the solubility of model compounds. For some aminodichlorotriazine derivatives, the problem of solubility at low temperatures proved unsolvable.^{11,12,15} Owing to the presence of fluorine in perfluoroalkoxy-1,3,5-triazine molecules, dynamic experiments can take advantage of ¹⁹F NMR spectroscopy, which requires less experimental time than ¹³C NMR and covers a broader range of chemical shifts than ¹H NMR, which is significant for shortening the experimental time.

Results and Discussion

Synthesis. Unsymmetrical symm-triazines were prepared by a procedure that makes it possible to avoid hydrolysis and transalkoxylation. The point is in the use of the lithium hydride base, which offers a number of advantages over aqueous solutions of alkali, carbonates, and bicarbonates or tertiary amines, which are used most often in the modification of chlorotriazines.^{23–29} The reaction of alcohols with lithium hydride is irreversible, giving the corresponding alkoxide and hydrogen. In addition, the reaction rate can be controlled by changing the grain size in the lithium hydride powder. Using this base, it is possible to create microconcentrations of the alkoxide, which allows one to take full advantage of the existing difference between the reactivities of di- and monochlorotriazines for selective replacement of one chlorine atom.

Published data on the synthesis and use of trifluoroethoxy-*symm*-triazines are few.^{30–34} We have not found any data on hexafluoroisopropoxy-*symm*-triazine derivatives; these triazine compounds were obtained for the first time. The yields of triazines 1-10 were 85-99%; the synthetic procedures are given in the Experimental.

Dynamic behavior. Amino-symm-triazines show hindered rotation about the exocyclic C–N bond (Scheme 1), which is partially double, due to the $n-\pi$ -conjugation of the lone pair of the amine nitrogen with the triazine ring.³⁵ The relatively high rotation barrier in aminotriazines can be attributed to the contribution of the dipolar canonical structures (see Scheme 1). The substituents R^1 , R^2 , R^3 , and R⁴ that stabilize these structures increase the barrier to hindered rotation. Dynamic effects in amino-symmtriazines with two identical substituents in the triazine ring have been detected previously $^{10-15}$ and described as the hindered internal rotation about the C-N bond. For arylamino-substituted symm-triazines with three different substituents in the triazine ring, similar effects are to be expected; however, the relative energies of the rotation isomers (conformers) may prove to be different, which would give rise to a non-degenerate exchange process¹² (Fig. 1).

It has been shown previously¹⁹ that at low temperatures, the ¹H and ¹³C NMR spectra of compound 1 exhibit two sets of signals corresponding to two rotation isomers, namely, conformers **A** and **B** (the arrow thickness reflects different electron-withdrawing characteristics of substituents in the triazine ring). For other *symm*-triazines with three different substituents (3–10), signals of different conformers in a ratio other than 1 : 1 are also observed. The structure of the major and minor conformers was determined using nuclear Overhauser effect experiments³⁶ (NOE).

DFT B3LYP calculations. The difference between the ground state energies of conformers **A** and **B** (see Fig. 1) is



due to the fact that one is energetically preferred over the other. A two-position non-degenerate exchange process

Scheme 1



corresponding to the rotation about the $N-C_{tr}$ bond was found in compound 1. NOE experiments have shown¹⁹ that conformer **A** predominates in an equilibrium mixture (see above).

In order to elucidate the molecule geometry in the ground and transition states and to calculate the hindered rotation barriers, we carried out DFT B3LYP/6-31G* quantum chemical calculations for some arylamino-*symm*-triazines. Several of transition states (TS) corresponding to the hindered rotation were identified. The calculation results are presented in Table 1.



Fig. 1. Hindered rotation in fully unsymmetrically substituted arylamino-*symm*-triazines (A and B are conformers, TS1 is the transition state); the thickness of the arrows reflects different electron-withdrawing characteristics of substituents in the triazine ring.

Table 1. Bond lengths (*d*) and sums of bond angles at the amine N atom ($\Sigma\omega$) in the ground states (conformer **A**) and in the transition state **TS1** during rotation about the N–C_{tr} bond and barriers to rotation about this bond (ΔG^{\neq}_{298}) found for *symm*-triazines **1**, **3**, **5**, **8**, and **10** by DFT B3LYP/6-31G* calculations

Com-	Ground state			Transition state TS1			
pound	d/Å		Σω	d/Å		Σω	ΔG_{298}^{\neq}
	N-C _{tr}	N-C _{Ar}	/deg	N-C _{tr}	N-C _{Ar}	/deg	/kJ mol ⁻¹
1	1.358	1.411	360.0	1.421	1.415	341.6	72.7
3	1.357	1.411	360.0	1.420	1.417	341.3	68.3
5	1.360	1.409	360.0	1.422	1.415	341.8	71.1
8	1.354	1.432	359.1	1.425	1.442	333.9	81.2
10	1.363	1.434	359.7	1.420	1.416	349.1	66.8

Structure of symm-triazines 1, 3, 5, 8, and 10 in conformations A and B. The conformers of symm-triazine 1 are shown in Fig. 2, a and b. The relative energies of the conformers are equal to within the accuracy of the calculation method.³⁷ It is noteworthy that in conformations A and B of molecule 1, the triazine ring, the NH group, and the benzene ring occur in one plane. The sum of the bond angles at the amine nitrogen atom (N(9), see Fig. 2, a and b) in these conformations is 360° (see Table 1). In conformer A, the C(6)—N(9) bond length (1.358 Å) is smaller than the C(11)-N(9) bond length (1.411 Å), *i.e.*, the order of the C(6)-N(9) bond is greater than the C(11)-N(9) bond order. Thus, the conjugation of the lone pair with the triazine ring is more efficient than that with the benzene ring. Similar data were obtained for conformer **B**, the C(6)-N(9) and C(11)-N(9) bond lengths being 1.359 and 1.411 Å, respectively.

According to DFT B3LYP/ $6-31G^*$ calculations, the other *symm*-triazines have a similar structure (see Table 1). Exceptions are compounds **8** and **10** in which the benzene



Fig. 2. Geometrical structure of the molecule of compound 1 in conformations A (*a*) and B (*b*) and in the transition states TS1 (*c*) and TS2 (*d*) corresponding to hindered rotation about the N– C_{tr} and N– C_{Ar} bonds, respectively.

ring of the aniline substituent does not lie in the same plane with the triazine ring. The N— C_{Ar} bonds in these molecules are longer than those in other compounds, *i.e.*, the lone pair is conjugated only with the triazine ring. In compound **8**, this appears to be due to the presence of two *ortho*-Me groups in the benzene ring, which create steric hindrances to the coplanar arrangement of the rings. In *symm*-triazine **10**, a coplanar arrangement of the rings is prevented by the Me group at the exocyclic nitrogen atom. The sums of the bond angles at the amine nitrogen in compounds **8** and **10** are less than 360° (see Table 1), *i.e.*, the N atom has a partially pyramidal structure.

Structure of the transition state TS1 to the rotation about the N–C_{tr} bond in compounds 1, 3, 5, 8, and 10. The results of calculation of the geometry of the transition state TS1, corresponding to the hindered rotation about the N–C_{tr} bond in compound 1, are shown in Fig. 2, c. In this transition state, the triazine ring and the substituents in the amino group occur in nearly perpendicular planes. Unlike the ground state of conformers A and B, in the transition state, the sum of the bond angles at exocyclic nitrogen is 341.6° (see Table 1). Since no n– π -conjugation with the triazine ring is present, the nitrogen lone pair in this transition state, as shown by calculations, is conjugated only with the benzene ring.

The N-C_{tr} bond in the transition state related to the rotation around this bond is substantially elongated compared with that in conformers **A** and **B**, being equal to 1.421 Å. The N-C_{Ar} bond length virtually does not change with respect to those in the ground states (1.415 Å). This bond is somewhat shorter than the N-C_{tr} bond, due to the conjugation between the nitrogen lone pair and the benzene ring.

The other *symm*-triazines studied by DFT B3LYP/6-31G* calculations have a similar structure in the transition state **TS1** (see Table 1). An exception is compound **8** in which no $n-\pi$ -conjugation with the benzene ring occurs in the transition state **TS1** due to the reasons outlined above. The sum of the bond angles at the amine nitrogen in its molecule is the smallest, while the N-C_{Ar} bond is the longest among the group of compounds in question (see Table 1). Hence, the aromatic ring of the aniline fragment in *symm*-triazine **8** does not show π -donor properties in either the ground state or the transition state **TS1**.

Charge distribution in the ground and transition states of compound 1. Comparison of the charge distribution in conformers A and B with that in the transition state to rotation about the $N-C_{tr}$ bond in compound 1 demonstrates that the transition state is less polar than the ground states (Table 2). Indeed, unlike conformers A and B, the TS1 state has overall charge of the same sign on the triazine and benzene rings, due to the back migration of the electron density to nitrogen and partly to the benzene ring. The foregoing can also be confirmed by

Table 2. Total charges on the triazine fragment (Σz_{tr}) , the Ph and NH groups $(\Sigma z_{Ph} \text{ and } \Sigma z_{NH}, \text{ respectively})$ in conformers **A** and **B** of the molecule of compound **1** and in the transition state **TS1** during rotation about the N–C_{tr} bond and changes in the charges relative to the state **TS1** ($\Delta\Sigma z$)

Conformer, state	$\Sigma z_{\rm tr}$	$\Delta \Sigma z_{\rm tr}$	$\Sigma z_{\rm Ph}$	$\Delta \Sigma z_{\rm Ph}$	$\Sigma z_{\rm NH}$	$\Delta \Sigma z_{\rm NH}$
A	-0.22	0.33	0.63	-0.41	-0.41	0.08
В	-0.22	0.33	0.63	-0.41	-0.41	0.08
TS1	0.11	0	0.22	0	-0.33	0

the negative activation entropy of the rotation ($\Delta S^{\neq} = -27.3 \text{ J mol}^{-1} \text{ K}^{-1}$). The negative ΔS^{\neq} values correspond to molecules with more polar ground state.³⁸ Thus, the calculations are in line with the negative ΔS^{\neq} value found experimentally¹⁹ for *symm*-triazine 1.

The transition state TS2 to the rotation around the $N-C_{Ar}$ bond in triazines 1, 3, 5, 8, and 10. The results of geometry calculations of the transition state TS2, corresponding to the rotation around the $N-C_{Ar}$ bond in compound 1, are shown in Fig. 2, *d*. In the transition state TS2, the benzene ring and the amino-group substituents occur almost in perpendicular planes. As in conformations A and B, the sum of the bond angles at the exocyclic nitrogen ($\Sigma\omega$) in the state TS2 amounts to 360°. Thus, the $n-\pi$ -conjugation with the benzene ring is not realized and, according to calculation results, the nitrogen lone pair in this transition state is involved in conjugation only with the triazine ring.

The N-C_{tr} bond in **TS2** is somewhat shorter than that in the initial conformers **A** and **B**, being equal to 1.355 Å. The N-C_{Ar} bond length is longer than that in the ground states, namely, 1.433 Å (see Table 1).

The barriers to rotation about the N–C_{tr} bond found by DFT B3LYP/6-31G* calculations are in the 67-81 kJ mol⁻¹ range, *i.e.*, they are somewhat higher than the earlier¹⁵ estimates of the rotation barriers in *symm*-triazines.

According to calculations, the barriers to rotation about the N–C_{Ar} bonds in the compounds under study (12–27 kJ mol⁻¹) are much lower than those about the N–C_{tr} bond, which is in line with the estimates of the barrier to rotation around this bond in *symm*-triazines reported previously¹⁵ (17 kJ mol⁻¹).

Thus, the DFT B3LYP/6-31G* calculations indicate that the barrier to rotation about the N– C_{tr} bond in anilino-*symm*-triazines is much higher than the barrier to rotation about the N– C_{Ar} bond.

The data obtained show that rotation about the N–C_{Ar} bond can be regarded as free, while rotation about the N–C_{tr} bond is hindered. The calculated heights of the barriers to rotation for the compounds in question are in 67-81 kJ mol⁻¹ range and do not differ much from the corresponding values for formamides.³⁹

Belyakov et al.

Table 3. Ratios of conformers A and B and energy differences (ΔG°) for fully unsymmetrically substituted *symm*-triazines 1, 3, 5, and 10

Com- pound	A : B	ΔG° /kJ mol ⁻¹		
1	1:0.51	1.2		
3	1:0.63	0.9		
5	1:0.50	1.6		
10	1:0.90	0.1		

Determination of the conformer ratio. The ratios and the relative energies of the conformers (ΔG°) of some fully unsymmetrically substituted *symm*-triazines are summarized in Table 3. The ΔG° value for the ethoxy derivative 5 is somewhat higher than that for 1 (see Table 3). The ethoxy group is more bulky than the methoxy group; therefore, the higher ratio of the conformers in compound 5 with respect to compound 1 cannot be attributed to steric factors. The steric factors do not have a substantial influence on the conformer ratio in *symm*-triazines, unlike those in other known⁴⁰ cases of hindered rotation about the C—N bond. The increase in the ΔG° value may be due to electronic factors, in particular, lower electron-withdrawing properties of the EtO group compared to the MeO group.

In the trifluoroethoxy derivative **3**, the difference between the conformer energies is smaller than this difference for compounds **5** and **1** (see Table 3). In this case, the steric factors do not, most likely, exert a substantial effect on the relative energies of the two conformers. The OCH₂CF₃ group is a strong electron acceptor with the constant $\sigma_I = 0.81$,⁴¹ which is much higher than these values for ethoxy and methoxy groups ($\sigma_I = 0.22-0.33$).⁴² The decrease in the energy difference between conformers **A** and **B** with respect to that in compound **1** or **5** can be attributed to more pronounced electron-withdrawing properties of the substituents in the triazine ring. In *N*-methylaniline derivative **10**, the ΔG° value is much lower than in aniline derivative **1** (see Table 3). The methyl group is more bulky than a hydrogen atom. According to calculations, the triazine and benzene rings in the ground state of compound **10**, unlike those in compounds **1**, **3**, and **5**, do not lie in one plane and no $n-\pi$ -conjugation of the nitrogen lone pair with the benzene ring is present. Nevertheless, even in this case, conformer **A** predominates in solution.

In a previous publication,¹⁹ we suggested that an intramolecular hydrogen bond may have an influence on the distribution of the conformers. The data obtained for *N*-methylaniline derivative **10** are inconsistent with this hypothesis. A conformer ratio other than 1 : 1 exists also in the absence of hydrogen in compound **10**. The introduction of electron-withdrawing substituents into the triazine ring results in a decrease in the conformer ratio. Nevertheless, the energy difference between conformers **A** and **B** observed experimentally is so small that currently it is impossible to draw definite conclusions concerning the reasons for higher stability of conformer **A** on the basis of the available calculation results.^{37,43}

Experimental determination of the barriers. In this study, the activation parameters of the hindered rotation in 1,3,5-triazines with different substituents were determined experimentally by LSA. The results of studies are given in Table 4.

The free activation energies for the hindered rotation in *symm*-triazines determined experimentally lie in the range of 59–77 kJ mol⁻¹. Note that the barriers found by the DFT B3LYP/6-31G* calculations are somewhat higher than those determined experimentally by dynamic NMR. Nevertheless, the calculation results are in good agreement with experimental data.

The rotation barrier in *N*-methyl-2,4,6-trinitroaniline is only 47.2 kJ mol⁻¹,⁴⁴ *i.e.*, the barriers to rotation in triazines are much higher than in anilines. This is attributable to the fact that the triazine ring is a stronger elec-

Com- pound	ΔH^{\neq} /kJ mol ⁻¹	Δ <i>S</i> ≠ /J mol ⁻¹ K ⁻¹	∆ <i>G</i> [≠] ₂₉₈ * /kJ mol ⁻¹	$\Delta T/K$	Monitored nucleus
1 2 3 4 5 6 7 8	57.4 ± 1.9 75.2 ± 1.1 65.8 ± 0.9 67.1 ± 0.4 55.3 ± 1.8 62.6 ± 3.2 68.9 ± 1.3 75.5 ± 2.5	$\begin{array}{r} -27.3\pm 6.5 \\ 54.3\pm 3.9 \\ -0.2\pm 3.0 \\ 19.3\pm 1.4 \\ -27.6\pm 5.4 \\ -18.1\pm 10.3 \\ 18.6\pm 4.7 \\ 2.8\pm 7.6 \end{array}$	65.6 59.0 65.8 61.4 63.5 68.0 63.4 76.6	$\begin{array}{c} 269 - 304 \\ 260 - 285 \\ 280 - 305 \\ 270 - 290 \\ 270 - 290 \\ 295 - 320 \\ 255 - 290 \\ 230 - 344 \end{array}$	¹³ C ¹³ C ¹⁹ F ¹⁹ F ¹³ C ¹⁹ F ¹ H
o 9 10	65.1±2.1 88.1±5.8	-3.8±7.0 9.6±7.7 87.0±20.7	62.3 62.2	265-285 273-287	¹ H ¹³ C

Table 4. Activation parameters of the hindered rotation about the $N-C_{tr}$ bond in symm-triazines 1-10

* Determination error is ± 0.8 kJ mol⁻¹.

tron acceptor than the benzene ring. The height of the barrier to hindered rotation about the C-N bond is most sensitive to the π -electron-withdrawing properties, because these properties determine the order of the bond around which the rotation takes place. Due to the presence of substituents (Cl, alkoxy group, and other), the triazine ring has stronger electron-withdrawing properties than the trinitrobenzene fragment. Previously, 45,46 a comparative study of the rotation barriers in dimethylaminosubstituted nitropyridines and pyrimidines has been carrier out. On the basis of the obtained results, the researchers concluded that the effect of one or several nitrogen atoms on the electron-withdrawing properties of the heterocyclic ring is comparable with the effect of introduction of a nitro group in the appropriate position of a carbon ring. In view of the rotation barriers in N-methyl-2,4,6-trinitroaniline, nitro-substituted pyrimidines, pyridines, and 1,3,5-triazines, the triazine ring is the strongest acceptor of the electron lone pair of the exocyclic nitrogen atom.

Note that hindered rotation in some of the *symm*-triazines studied is characterized by great absolute magnitudes of ΔS^{\ddagger} . On the basis of calculations, these ΔS^{\ddagger} values can be explained by assuming that the ground state is more polar than the transition state in the case of negative activation entropies. Conversely, high positive values of the activation enthalpy are attributed to less polar ground state compared to the transition state.³⁸ It has been shown above that in compound 1, the high negative activation entropy is in good agreement with the calculated results. The ΔS^{\ddagger} value in *N*-methyl-2,4,6-trinitroaniline is also rather high and amounts to 39 J mol⁻¹ K⁻¹.

The effect of the structure of the aromatic substituent on the barrier height. According to experimental data, the rotation around the N-CAr bond remains free on the NMR time scale. It can be hampered due to $n-\pi$ -conjugation of the lone pair of the exocyclic nitrogen atom with the aryl substituent. According to calculation results, the barrier to rotation around this bond in compound 1 is 13.4 kJ mol⁻¹. By comparing the heights of the rotation barrier for compounds 3 and 8, one can estimate quantitatively the energy of interaction between the exocyclic nitrogen lone pair and the aryl group. The presence of ortho-methyl groups in the aniline ring of compound 8 is an essential steric hindrance to a coplanar arrangement of the triazine and benzene rings. According to calculations, this should result in a pronounced increase in the N-C_{Ar} bond length accompanied by some decrease in the $N\!-\!C_{tr}$ bond length (see Table 1). The ΔG_{298}^{\neq} value for compound **8** is 11 kJ mol⁻¹ higher than that for compound **3** and is comparable with this value for dichloroalkylaminosymm-triazines.¹² Based on the calculations, this pronounced increase in the rotation barrier can be ascribed to the fact that two bulky groups in the ortho-positions of the aromatic ring preclude the effective $n-\pi$ -conjugation of the lone electron pair of the exocyclic nitrogen with the benzene ring. Hence, the $n-\pi$ -conjugation with the triazine ring becomes predominant and the $N-C_{tr}$ bond order increases, giving rise to a higher barrier to rotation about this bond. Without $n-\pi$ -conjugation with the arylamine group, this group can be represented as a bulky alkylamine group, as indicated by the similarity of the activation parameters of the hindered rotation, which are 76.6 and 78 kJ mol⁻¹ for compound **8** and dichloro-octylamino-*symm*-triazine,¹² respectively. Thus, the value of 11 kJ mol⁻¹ determined experimentally can serve as a quantitative measure of the energy of $n-\pi$ -conjugation of the lone electron pair of the exocyclic nitrogen with the aromatic group. This value is in good agreement with the calculation results.

Note that in those cases where the substituents in the aniline fragment do not violate the planar structure of the triazine—aniline substituent system (*cf.* ΔG^{\neq}_{298} for compounds **2**, **9**, and **10**; see Table 4), the barrier height does not change much. A quantitative estimation of the effect of substituents in the arylamino fragment on the height of the rotation barrier will be given elsewhere.

The effect of substituents in the triazine ring on the height of the hindered rotation barriers. The electron-withdrawing properties of the groups R³ and R⁴ influence the height of the rotation barrier in arylamino-symm-triazines.¹¹ Comparison of the changes in the ΔG^{\neq}_{298} values for the pairs of compounds 2 and 1, 3 and 4, and 6 and 7 (see Table 4) provides the following conclusion: the replacement of the chlorine atom in the triazine ring by the MeO group entails a decrease in the barrier to hindered rotation. This is in line with the previous data¹¹ on variation of the rotation barriers in bis- and tris(N,N-dialkylamino)-symm-triazines. A decrease in the barrier may be due to the decrease in the electronegative effect of the triazine ring upon the replacement of the chlorine atom by the less electronegative methoxy group.¹¹ This is accompanied by a decrease in the electron density on the N-C_{tr} bond, inducing a decrease in the barrier to rotation about this bond.

The NMR spectra of fully unsymmetrically substituted 1,3,5-triazines exhibit a non-degenerate two-position exchange process, representing the hindered rotation about the N— C_{tr} bond. Using quantum chemical calculations, the geometries and the relative energies of the ground and transition states were calculated. It was found that conformer A predominates in an equilibrium mixture for *symm*-triazines **3**—**10** (see above). However, the energy difference between the conformers observed experimentally is so minor that no categorical conclusions concerning the reasons for higher stability of conformer A can be currently drawn based on the calculation results. Presumably, the energy difference between the conformers is related to different electron-withdrawing properties of the groups in the triazine ring. The activation parameters for the hindered rotation in ten *symm*-triazines were measured experimentally. The barrier heights are in good agreement with the calculation results.

This communication opens a series of publications devoted to the synthesis, structure, and dynamic behavior in solution of arylamino-1,3,5-triazines. This paper gives an account of studies dealing with unsymmetrically substituted arylamino-1,3,5-triazines. The theoretical section is an attempt to estimate the scope of the DFT B3LYP/6-31G* quantum chemical calculations for the studies of hindered rotation in *symm*-triazines. The use of other methods and basis sets for taking into account the electron correlation is the subject of further theoretical studies. The subsequent publications are planned to consider the behavior of arylamino-1,3,5-triazines containing substituents in the aniline fragment, *para*-substituted arylamino-1,3,5-triazines, and to study the entropy—enthalpy compensation.

Experimental

The ¹H, ¹³C–{¹H}, and ¹⁹F–{¹H} NMR spectra were recorded by standard procedures on Bruker AM-300, Bruker WM-250, and Bruker AC-200 spectrometers. Dynamic NMR experimental series were carried out using the Global-DNMR software we developed.⁴⁷ For each compound, seven to twelve points were recorded in the range from 20–30 °C below the coalescence point to 10–15 °C above coalescence point. For NMR experiments, solutions of compounds in a methylene dichloride—chloroform—carbon tetrachloride (60 : 27 : 13) system were used; this solvent mixture allowed working in a broad temperature range. The NOE experiments for compounds 1, 3, 5, and 10 were carried out at –23 °C. The conformer ratio in fully unsymmetrically substituted triazines was determined under standard conditions based on the NMR integral intensities

$$R = I_{\text{mai}}/I_{\text{min}},$$

where R is the conformer ratio, I_{maj} and I_{min} are the integral intensities of the signals from the major and minor conformers, respectively.

The melting points were measured on a Boetius hot stage with a heating rate of 4 °C min⁻¹ at the melting point. Mass spectra were recorded on a Varian CH-6 instrument with direct sample injection into the ion source at an ionizing electron energy of 70 eV, an accelerating voltage of 1.75 kV, and an emission current of 100 mA. The molecular ion peaks and fragment ions from chlorine-containing compounds 1, 3, 5, and 8–10 refer to ³⁵Cl.

The results of the NMR experiments were processed using standard Bruker software (DISNMR on ASPECT-3000 operating under Adakos, XWINNMR on IBM-compatible PC operating under Linux) and the programs we developed for recording and automated processing the DNMR spectra (Global-DNMR).⁴⁷

All procedures for conversion of the spectra into various data formats were carried out using the CODER7 program.⁴⁸

For LSA, the signals of the alkoxy and fluoroalkoxy substituents in the 1 H, 13 C, and 19 F NMR spectra were used. The calculations were carried out using the DYNNMR program,¹⁰ which iterates the intensities, the resonance frequencies of the exchanging signals, and the lifetimes in particular states. The cross-relaxation times were measured in each temperature point.

The geometry optimization and the calculation of the energy of *symm*-triazines was carried out using the B3LYP hybrid potential^{49–51} in the standard 6-31G* basis set.⁵² This method ensures a sufficient accuracy of calculations compared with other methods.⁴³ The character of the stationary points found was checked by calculating the eigen values of the matrix of the second derivatives of energy (the absence of imaginary frequencies for the ground states and the presence of one imaginary frequency for the transition states). The atom charges were calculated by the Mulliken method. The thermodynamic functions were determined within the harmonic oscillator—rigid rotator model. All calculations were performed using the Gaussian 98 software.⁵³ For visualization of molecular structures and vibrations, the MOLDEN graphical package was used.⁵⁴

2-Chloro-4-methoxy-6-phenylamino-1,3,5-triazine (1). 2,4-Dichloro-6-phenylamino-1,3,5-triazine (5 g, 20.75 mmol), synthesized by known procedures, $^{23-26}$ was dissolved in methanol (50 mL) and cooled to 0 °C on an ice bath. A lithium hydride coarse powder (grain size 1-2 mm) (190 mg, 23.75 mmol) was added with stirring, the mixture was stirred for 2.5 h (the product may precipitate during the reaction), and the bath was removed. The reaction mixture was left for ~14 h, diluted with water, and filtered. The precipitate was dried on the filter to as constant weight. Yield 4.70 g (95.8%), m.p. 140-141 °C (methanol). Found (%): C, 50.78; H, 3.88; Cl, 14.52; N, 24.12. C₁₀H₉ClN₄O. Calculated (%): C, 50.75; H, 3.83; Cl, 14.98; N, 23.67. ¹H NMR (DMSO-d₆), δ: 3.95 (s, 3 H, OMe); 7.12 (m, 1 H, H arom.); 7.35, 7.68 (both m, 2 H each, H arom.); 10.58 (br.s, 1 H, NH). MS, m/z (I_{rel} (%)): 236 [M]⁺ (86); 235 $[M - H]^+$ (100); 201 $[M - Cl]^+$ (18); 159 $[M - C_6H_5]^+$ (10); 159 $[M - C_6H_5NH]^+$ (23); 118 $[C_6H_5NHCN]^+$ (42); 91 $[C_6H_5N]^+$ (25); 77 $[C_6H_5]^+$ (60).

2,4-Dimethoxy-6-phenylamino-1,3,5-triazine (2). 2,4-Dichloro-6-phenylamino-1,3,5-triazine (2.41 g, 10 mmol) was dissolved in methanol (50 mL), lithium hydride fine powder (240 mg, 30 mmol) was added with cooling and stirring and the mixture was left for ~14 h. Methanol was evaporated on a rotary evaporator, the residue was washed with water and dried on a filter to a constant weight. Yield 1.98 g (85.5%), m.p. 134–135 °C (methanol) (*cf.* Ref. 27: m.p. 133–134 °C (methanol–water)).

2-Chloro-6-phenylamino-4-(2.2.2-trifluoroethoxy)-1.3.5-triazine (3). 2,4-Dichloro-6-phenylamino-1,3,5-triazine²³⁻²⁶ (2.41 g, 10.0 mmol) was dissolved in anhydrous THF (10 mL), 2,2,2-trifluoroethanol (2.5 mL, 34.3 mmol) was added, the mixture was cooled to 0 °C on an ice bath, a lithium hydride coarse powder (grain size 1-2 mm) (100 mg, 12.5 mmol) was added with stirring, the mixture was stirred for an additional 2.5 h, and the bath was removed. The reaction mixture was left for ~14 h, diluted with water, and filtered. The precipitate was dried on the filter to a constant weight. Yield 2.9 g (95.2%), m.p. 125-126 °C (heptane). Found (%): C, 43.41; H, 2.86; N, 18.34. C₁₁H₈ClF₃N₄O. Calculated (%): C, 43.37; H, 2.63; N, 18.39. ¹H NMR (DMSO-d₆), δ: 5.02 (q, 2 H, OCH₂); 7.15 (m, 1 H, H arom.); 7.37, 7.65 (both m, 2 H each, H arom.); 10.84 (br.s, 1 H, NH). MS, m/z (I_{rel} (%)): 304 [M]⁺ (91); 303 [M - H]⁺ (100); 285 $[M - F]^+$ (5); 269 $[M - C1]^+$ (15); 205

$$\begin{split} & [M - OCHCF_3]^+ \ (10); \ 185 \ [(M - NCNHC_6H_5) - H]^+ \ (12); \\ & 144 \ [269 - CNOCH_2CF_3]^+ \ (35); \ 118 \ [NCNHC_6H_5]^+ \ (45); \ 91 \\ & [C_6H_5N]^+ \ (15); \ 77 \ [C_6H_5]^+ \ (35); \ 69 \ [CF_3]^+ \ (10). \end{split}$$

2-Methoxy-6-phenylamino-4-(2,2,2-trifluoroethoxy)-1,3,5triazine (4). 2-Chloro-4-methoxy-6-phenylamino-1,3,5-triazine (2.37 g, 10 mmol) was added with stirring at room temperature to a solution of lithium 2,2,2-trifluoroethoxide (from 2.5 mL of 2,2,2-trifluoroethanol and 274 mg of finely powdered lithium hydride, 34.3 mmol each) in anhydrous THF (15 mL). The mixture was left for ~14 h, the solvents were evaporated, and the residue was washed with water and dried on the filter to a constant weight. Yield 2.9 g (96.7%), m.p. 126-127 °C (heptane). Found (%): C, 47.62; H, 3.76. C₁₂H₁₁F₃N₄O₂. Calculated (%): C, 48.00; H, 3.69. ¹H NMR (DMSO-d₆), δ: 3.95 (s, 3 H, OMe); 4.98 (q, 2 H, OCH₂); 7.07 (m, 1 H, H arom.); 7.33, 7.68 (both m, 2 H each, H arom.); 10.16 (br.s, 1 H, NH). MS, m/z (I_{rel} (%)): $300 [M]^+ (85); 299 [M - H]^+ (100); 281 [M - F]^+ (7); 269$ [M – OCH₃]⁺ (7); 201 [M – OCHCF₃]⁺ (5); 159 [C₈H₅N₃O]⁺ (15); 118 $[NCNHC_6H_5]^+$ (15); 91 $[C_6H_5N]^+$ (5); 77 $[C_6H_5]^+$ $(10); 69 [CF_3]^+ (5).$

2-Chloro-4-ethoxy-6-phenylamino-1,3,5-triazine (5). 2,4-Dichloro-6-phenylamino-1,3,5-triazine²³⁻²⁶ (2.41 g, 10.0 mmol) was dissolved in ethanol (30 mL), the solution was cooled to 0 °C on an ice bath, a lithium hydride coarse powder (grain size 1-2 mm) (100 mg, 12.5 mmol) was added with stirring, the mixture was stirred for 2.5 h (during the reaction, the product may precipitate), and the bath was removed. The reaction mixture was left for ~14 h, diluted with water, and filtered. The precipitate was dried on the filter to a constant weight. Yield 2.31 g (92.2%), m.p. 103-104 °C (heptane). Found (%): C, 52.93; H, 4.43; Cl, 14.15; N, 22.26. C₁₁H₁₁ClN₄O. Calculated (%): C, 52.71; H, 4.42; Cl, 14.14; N, 22.35. ¹H NMR (DMSO-d₆), δ: 1.34 (t, 3 H, Me); 4.40 (q, 2 H, OCH₂); 7.12 (m, 1 H, H arom.); 7.37, 7.68 (both m, 2 H each, H arom.); 10.55 (br.s, 1 H, NH). MS, *m/z* (*I*_{rel} (%)): 250 $[M]^+$ (83); 249 $[M - H]^+$ (30); 221 $[M - C_2H_5]^+$ (72); 205 $[M - OC_2H_5]^+$ (28); 186 $[221 - Cl]^+$ (25); 144 $[186 - CNO]^+$ (35); 118 $[C_6H_5NHCN]^+$ (77); 91 $[C_6H_5N]^+$ (30); 77 $[C_6H_5]^+$ (100).

2-Chloro-4-(1,1,1,3,3,3-hexafluoroprop-2-oxy)-6-phenylamino-1,3,5-triazine (6). 2,4-Dichloro-6-phenylamino-1,3,5triazine²³⁻²⁶ (2.41 g, 10.0 mmol) was dissolved in anhydrous THF (10 mL), 1,1,1,3,3,3-hexafluoropropan-2-ol (5 mL, 47.5 mmol) was added, the mixture was cooled to 0 °C on an ice bath, a lithium hydride coarse powder (grain size 1-2 mm) (100 mg, 12.5 mmol) was added with stirring, the mixture was stirred for 2.5 h, and the bath was removed. The reaction mixture was left for ~14 h, diluted with water, and extracted with ether (100 mL). The extract was dried with calcined sodium sulfate, and ether was evaporated to give 3.5 g (94.0%) of the target product as a thick oil contaminated by a minor amount (<5%) of 2,4-di(1,1,1,3,3,3-hexafluoroprop-2-oxy)-6-phenylamino-1,3,5-triazine, which could not be separated by chromatography due to little difference between the $R_{\rm f}$ values of these compounds. ¹H NMR (DMSO-d₆), δ : 6.94 (m, 1 H, OCH); 7.18 (m, 1 H, H arom.); 7.40, 7.61 (both m, 2 H each, H arom.); 11.09 (br.s, 1 H, NH).

2-Methoxy-4-(1,1,1,3,3,3-hexafluoroprop-2-oxy)-6-phenylamino-1,3,5-triazine (7). 2-Chloro-4-methoxy-6-phenylamino-1,3,5-triazine (2.37 g, 10 mmol) was added with stirring at room temperature to a solution of lithium 1,1,1,3,3,3-hexafluoroprop-2-oxide (from 2.5 mL of 1,1,1,3,3,3-hexafluoropropan-2-ol and 195 mg of finely dispersed lithium hydride powder, 24.4 mmol each) in anhydrous THF (15 mL), the mixture was left for ~14 h, the solvent was evaporated, and the residue was washed with water and dried on the filter to a constant weight. Yield 3.5 g (95%), m.p. 82–83 °C (methanol). Found (%): C, 42.54; H, 2.83; N, 15.13. $C_{13}H_{10}F_6N_4O_2$. Calculated (%): C, 42.40; H, 2.74; N, 15.21. ¹H NMR (DMSO-d₆), δ : 3.99 (s, 3 H, OMe); 6.94 (m, 1 H, OCH); 7.12 (m, 1 H, H arom.); 7.37 (m, 2 H, H arom.); 7.68 (br.m, 2 H, H arom.); 10.44 (br.s, 1 H, NH). MS, m/z (I_{rel} (%)): 368 [M]⁺ (89); 367 [M – H]⁺ (100); 349 [M – F]⁺ (10); 201 [M – OCH(CF₃)₂]⁺ (16); 159 [C₈H₅N₃O]⁺ (50); 118 [NCNHC₆H₅]⁺ (45); 91 [C₆H₅N]⁺ (15); 77 [C₆H₅]⁺ (25); 69 [CF₃]⁺ (32).

2-Chloro-6-(2,6-dimethylphenylamino)-4-(2,2,2-trifluoroethoxy)-1,3,5-triazine (8). 2,4-Dichloro-6-(2,6-dimethylphenylamino)-1,3,5-triazine (2.69 g, 10 mmol) synthesized by a known procedure²⁸ was dissolved in anhydrous THF (10 mL), 2,2,2-trifluoroethanol (5 mL, 68.6 mmol) was added, the mixture was cooled to 0 °C on an ice bath, and a lithium hydride coarse powder (grain size 1-2 mm) (100 mg, 12.5 mmol) was added with stirring. The mixture was stirred for 2.5 h, and the bath was removed. The reaction mixture was left for ~14 h, diluted with water, and filtered. The precipitate was dried on the filter to a constant weight. Yield 3.3 g (99.2%), m.p. 160-161 °C (heptane). Found (%): C, 46.71; H, 3.64; N, 16.97. C₁₃H₁₂ClF₃N₄O. Calculated (%): C, 46.93; H, 3.64; N, 16.84. ¹H NMR (DMSO- d_6), δ : 2.13 (s, 6 H, 2 Me); 4.40, 5.04 (q, 2 H, OCH₂, ratio 56 : 44); 7.13 (m, 3 H, H arom.); 10.05, 10.15 (br.s, 1 H, NH, ratio 44 : 56). MS, m/z (I_{rel} (%)): 332 [M]⁺ (50); 317 $[M - CH_3]^+$ (48); 297 $[M - Cl]^+$ (15); 249 $[M - CH_2CF_3]^+$ (61); 212 $[M - C_8 H_9 NH]^+$ (25); 186 $[M - C_8 H_9 NHCN]^+$ (5); 145 $[C_8H_0NCN]^+$ (100); 118 $[C_8H_0NCN - HCN]^+$ (30); 91 $[C_6H_5N]^+$ (40); 77 $[C_6H_5]^+$ (50).

2-Chloro-6-(biphenyl-2-ylamino)-4-methoxy-1,3,5-triazine (9). 6-(Biphenyl-2-ylamino)-2,4-dichloro-1,3,5-triazine (3.17 g, 10.0 mmol), synthesized by a known procedure²⁶ from cyanuric chloride and 2-aminobiphenyl, was dissolved in ethanol (50 mL), the solution was cooled to 0 °C on an ice bath, and a lithium hydride coarse powder (grain size 1-2 mm) (100 mg, 12.5 mmol) was added with stirring, the mixture was stirred for 2.5 h (the product may precipitate during the reaction), and the bath was removed. The reaction mixture was left for ~14 h, diluted with water, and filtered. The precipitate was dried on the filter to a constant weight. Yield 3.0 g (96.0%), m.p. 99-100 °C (heptane). Found (%): C, 61.90; H, 4.13; Cl, 10.77; N, 18.19. C₁₆H₁₃ClN₄O. Calculated (%): C, 61.45; H, 4.19; Cl, 11.31; N, 17.91. ¹H NMR (DMSO-d₆), δ: 3.50 (s, 3 H, OMe); 7.38 (m, 9 H, H arom.); 9.95 (br.s, 1 H, NH). MS, *m/z* (*I*_{rel} (%)): 312 $[M]^+$ (100); 311 $[M - H]^+$ (36); 277 $[M - Cl]^+$ (32); 235 $[M - C_6H_5]^+$ (49); 220 $[235 - CH_3]^+$ (49); 193 $[C_{12}H_9NCN]^+$ (21); 178 $[235 - CH_3OCN]^+$ (80); 167 $[C_{12}H_9N]^+$ (49); 152 $[178 - CN]^+$ (25); 77 $[C_6H_5]^+$ (12).

2-Chloro-4-methoxy-6-[(*N*-methyl)phenylamino]-1,3,5-triazine (10). 2,4-Dichloro-6-[(*N*-methyl)phenylamino]-1,3,5triazine (2.59 g, 10.0 mmol), synthesized by a known procedure,²⁹ was dissolved in methanol (50 mL), cooled to 0 °C on an ice bath, and a lithium hydride coarse powder (grain size 1-2 mm) (190 mg, 23.75 mmol) was added with stirring, the mixture was stirred for 2.5 h (the product may precipitate during the reaction), and the bath was removed. The reaction mixture was left for ~14 h, diluted with water, and filtered. The precipitate was dried on the filter to a constant weight. Yield 2.30 g (92%), m.p. 103-104 °C (heptane). Found (%): C, 52.72; H, 4.39; Cl, 14.51; N, 22.35. C₁₁H₁₁ClN₄O. Calculated (%): C, 52.70; H, 4.42; Cl, 14.14; N, 22.35. ¹H NMR (DMSO-d₆), 297 K, δ: 3.50 (s, 3 H, NMe); 3.70 (br.s, 3 H, OMe); 7.32, 7.45 (m, 5 H, H arom.). ¹H NMR (CDCl₃), 297 K, δ: 3.52 (s, 3 H, NMe); 3.76, 4.00 (br. s, 3 H, OMe); 7.32, 7.45 (m, 5 H, H arom.). ¹H NMR (CDCl₃), 230 K, δ: 3.52 (s, 3 H, NMe); 3.76, 4.05 (s, 3 H, OMe); 7.32, 7.45 (m, 5 H, H arom.). ¹³C NMR (CDCl₃), δ: 171.23, 170.72 (C(2) and C(4) triazine); 166.35 (C(6) triazine); 143.00, 129.80, 127.74, 126.70 (C₆H₅); 56.05, 55.90 (OMe (conformers)); 39.58, 39.40 (NMe (conformers)). MS, m/z (I_{rel} (%)): 250 [M]⁺ (48); 249 [M - H]⁺ (100); 235 $[M - CH_3]^+$ (3); 173 $[M - C_6H_5]^+$ (9); 158 $[235 - C_6H_5]^+$ (5); 131 $[CH_2NCNC_6H_5]^+$ (20); 106 $[CH_3NC_6H_5]^+$ (28); 77 $[C_6H_5]^+$ (22).

The authors are grateful to V. P. Ananikov for assistance in the calculations using the Gaussian software and interpretation of the results.

References

- 1. I. A. Godunov and V. M. Tatevskii, *Zh. Fiz. Khim.*, 1995, **69**, 141 [*Russ. J. Phys. Chem.*, 1995, **69** (Engl. Transl.)].
- E. M. Smolin and L. Rappoport, *Heterocycl. Compd.*, Wiley, New York—London, 1959, XIII, 168.
- H. Inoue, S. Ohki, E. Kotaka, N. Kuboyama, A. Ohki, K. Koizumi, H. Kohno, P. Boger, and K. Wakabayashi, *J. Pestic. Sci.*, 2000, 25, 101.
- N. Kuboyama, K. Kozumi, S. Ohki, and K. Wakabayashi, J. Pestic. Sci., 1998, 23, 268.
- Y. Iino, T. Karakida, N. Sugamata, T. Andoh, H. Takei, M. Takahashi, S. Yaguchi, Y. Matsuno, M. Takehara, M. Sakato, S. Kawashima, and Y. Morishita, *Anticancer Res.*, 1998, 18, 171.
- M. Falorni, G. Giacomelli, L. Mameli, and A. Porcheddu, *Tetrahedron Lett.*, 1998, **39**, 7607.
- M. Kunishima, C. Kawachi, J. Morita, K. Terao, F. Iwasaki, and S. Tani, *Tetrahedron*, 1999, 55, 13159.
- 8. J.-Y. Su, X.-H. Xu, L.-M. Zeng, M.-Y. Wang, N. Lu, Y. Lu, and Q.-T. Zhang, *Phytochemistry*, 1998, **48**, 583.
- 9. I. Ujvary, Pest. Management Sci., 2000, 56, 703.
- A. V. Shastin, T. I. Godovikova, S. P. Golova, M. V. Povorin, D. E. Dmitriev, M. O. Dekaprilevich, Yu. A. Strelenko, Yu. T. Struchkov, L. I. Khmel'nitskii, and B. L. Korsunskii, *Khim. Geterotsikl. Soedin.*, 1995, 679 [*Chem. Heterocycl. Compd.*, 1995 (Engl. Transl.)].
- A. R. Katritzky, I. Chiviriga, P. J. Steel, and D. C. Oniciu, J. Chem. Soc., Perkin Trans 2, 1996, 443.
- S. A. Brewer, H. T. Burnell, I. Holden, B. G. Jones, and C. R. Willis, J. Chem. Soc., Perkin Trans 2, 1999, 1231.
- V. M. Rumjanek, J. B. N. da Costa, A. Echevarria, and M. F. Cavalcante, *Struct. Chem.*, 2000, **11**, 303.
- M. Amm, N. Platzer, J. Guilhem, J. P. Bouchet, and J. P. Volland, *Magn. Reson. Chem.*, 2001, 39, 77.
- H. E. Birkett, R. K. Harris, P. Hodgkinson, K. Carr, M. H. Charlton, J. C. Cherryman, A. M. Chippendale, and R. P. Glover, *Magn. Reson. Chem.*, 2000, 38, 504.

- A. V. Popov, A. V. Shastin, E. L. Luzina, A. N. Pushin, and T. N. Gavrishova, *Izv. Akad. Nauk. Ser. Khim.*, 1999, 1568 [*Russ. Chem. Bull.*, 1999, **48**, 1548 (Engl. Transl.)].
- N. M. Emanuel' and D. G. Knorre, *Kurs khimicheskoi kinetiki [Course of Chemical Kinetics*], Vysshaya shkola, Moscow, 1969, 65 (in Russian).
- M. V. Gorelik and L. S. Efros, Osnovy khimii i tekhnologii aromaticheskikh soedinenii [Foundations of the Chemistry and Technology of Aromatic Compounds], Khimiya, Moscow, 1992, 32 (in Russian).
- P. A. Belyakov, A. V. Shastin, and Yu. A. Strelenko, *Izv. Akad. Nauk. Ser. Khim.*, 2001, 2361 [*Russ. Chem. Bull., Int. Ed.*, 2001, **50**, 2473 (Engl. Transl.)].
- 20. R. A. Sack, Mol. Phys., 1958, 1, 163.
- K. Spaargaren, P. K. Korver, P. Van-der Haak, and Th. de Boer, J. Org. Magn. Reson., 1971, 3, 615.
- T. Drakenberg, K.-I. Dahlquist, and S. Forsen, Acta Chem. Scand., 1970, 24, 694.
- K. R. Desai and M. M. Pathak, J. Indian Chem. Soc., 1985, 62, 168.
- 24. J. T. Thurston, J. R. Dudley, D. W. Kaiser, I. Hechenbleicner, F. C. Schaefer, and D. Holm-Hansen, J. Am. Chem. Soc., 1955, 77, 5918.
- 25. W. Cuthbertson and J. Moffat, J. Chem. Soc., 1948, 561.
- 26. N. V. Kozlova, D. F. Kutepov, D. N. Khokhlov, and A. I. Krymova, *Zh. Obshch. Khim.*, 1963, **33**, 3304 [*J. Gen. Chem. USSR*, 1963, **33** (Engl. Transl.)].
- 27. G. Rembarz, E. Fischer, and P. Neels, J. Prakt. Chem., 1975, 317, 293.
- 28. J. M. Patel, M. P. Dave, and K. A. Thaker, J. Inst. Chem. India, 1984, 56, 165.
- 29. J. T. Thurston, J. R. Dudley, D. W. Kaiser, I. Hechenbleicner, F. C. Schaefer, and D. Holm-Hansen, J. Am. Chem. Soc., 1951, 73, 2981.
- 30. A. V. Kashkin, E. P. Krylova, and F. A. Baibikov, *Zh. Prikl. Khim.*, 1975, 1329 [*J. Appl. Chem. USSR*, 1975, 6 (Engl. Transl.)].
- A. V. Kashkin, F. A. Baibikov, and E. N. Krylova, *Zh. Org. Khim.*, 1976, 1329 [*J. Org. Chem. USSR*, 1976, **12** (Engl. Transl.)].
- 32. A. J. Matuszko and M. S. Chang, J. Org. Chem., 1965, 30, 3724.
- 33. W. M. Koppes and H. G. Adolph, J. Org. Chem., 1981, 46, 406.
- 34. M. D. Nicholson and G. A. Roy, US Pat. 4704159; Chem. Abstrs, 1986, 104, 148904j.
- 35. G. M. Pogosyan, V. A. Pankratov, V. N. Zaplishnyi, and S. G. Matsoyan, *Politriaziny [Polytriazines]*, Izd-vo Akad. Nauk Arm. SSR, Erevan, 1987, 13 (in Russian).
- 36. J. H. Noggle and R. E. Shirmer, *The Nuclear Overhauser Effect. Chemical Applications*, Academic Press, New York, 1971, 266 pp.
- 37. J. M. Martell, J. D. Goddard, and L. A. Eriksson, J. Phys. Chem. A, 1997, 101, 1927.
- 38. J. Sandstrom and I. Wennerbeck, *Acta Chem. Scand.*, 1971, 24, 1191.
- H. E. Birkett, J. C. Cherryman, A. M. Chippendale, P. Hazendonk, and R. K. Harris, J. Mol. Struct., 2002, 602, 59.
- 40. T. Ozawa, Y. Isoda, H. Watanabe, T. Yuzuri, H. Suezawa, K. Sakakibara, and M. Hirota, *Magn. Reson. Chem.*, 1997, 35, 323.

- 41. R. Knorr, Tetrahedron, 1981, 37, 929.
- 42. A. N. Vereshchagin, Induktivnyi effekt. Konstanty zamestitelei dlya korrelyatsionnogo analiza [Inductive Effect. Constants of Substituents for Correlation Analysis], Nauka, Moscow, 1988, 26 pp. (in Russian).
- 43. W. Koch and M. C. Holthausen, A Chemist's Guide to Density Functional Theory, Weinheim, New York, 2001.
- 44. J. Heidberg, J. A. Weil, G. A. Janusonis, and J. K. Anderson, J. Chem. Phys., 1964, 41, 1033.
- 45. J. von Jouanne and J. Heidberg, J. Am. Chem. Soc., 1973, 95, 487.
- 46. A. R. Katrizky and G. J. T. Tiddy, Org. Magn. Reson., 1969, 1, 57.
- 47. P. A. Belyakov, Ph.D. Thesis (Chem.), N. D. Zelinsky Inst. Org. Chem., Russian Academy of Sciences, Moscow, 2003 (in Russian).
- 48. A. O. Krasavin, CODER7, http://nmr.ioc.ac.ru/coder7.zip.
- 49. A. D. Becke, Phys. Rev. A, 1988, 38, 3098.
- 50. C. Lee, W. Yang, and R. G. Parr, Phys. Rev. B, 1988, 37, 785.
- 51. A. D. Becke, J. Chem. Phys., 1993, 98, 5648.
- 52. R. Ditchfield, W. J. Hehre, and J. A. Pople, *J. Chem. Phys.*, 1971, **54**, 724.
- 53. M. J. Frisch, G. W. Trucks, H. B. Schlegel, G. E. Scuseria, M. A. Robb, J. R. Cheeseman, V. G. Zakrzewski, J. A. Montgomery, Jr., R. E. Stratmann, J. C. Burant, S. Dapprich, J. M. Millam, A. D. Daniels, K. N. Kudin, M. C. Strain, O. Farkas, J. Tomasi, V. Barone, M. Cossi, R. Cammi, B. Mennucci, C. Pomelli, C. Adamo, S. Clifford, J. Ochterski, G. A. Petersson, P. Y. Ayala, Q. Cui, K. Morokuma, D. K. Malick, A. D. Rabuck, K. Raghavachari, J. B. Foresman, J. Cioslowski, J. V. Ortiz, B. B. Stefanov, G. Liu, A. Liashenko, P. Piskorz, I. Komaromi, R. Gomperts, R. L. Martin, D. J. Fox, T. Keith, M. A. Al-Laham, C. Y. Peng, A. Nanayakkara, C. Gonzalez, M. Challacombe, P. M. W. Gill, B. Johnson, W. Chen, M. W. Wong, J. L. Andres, C. Gonzalez, M. Head-Gordon, E. S. Replogle, and J. A. Pople, Gaussian 98, Gaussian Inc., Pittsburgh (PA), 1998.
- 54. G. Schaftenaar and J. H. Noordik, J. Comput.-Aided Mol. Des., 2000, 14, 123.

Received October 21, 2004; in revised form September 7, 2005