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Prediction of the Phase Type Based on Computer Simulation of Molecular Ordering in Nitrogen-Containing Heterocyclic Compounds

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Abstract—Computer simulation 3,6-bis(4-butylphenyl)-1,2,4,5-tetrazine, 2,5-bis(4-butylphenyl)pyrazine, 2,5-bis(4-butylphenyl)pyrimidine and 3,6-bis(4-butylphenyl)pyridazine dimers differing in the configuration has been performed. The molecular ordering was estimated basing on the molecular movements dynamics in dimers over a range of temperature. It has been shown that coefficients of translational rigidity can serve as efficient measure to determine the relationship between the compounds structure and their phase properties. The value of the rigidity coefficient has been found to quantitatively characterize the type of the phase (crystalline, liquid-crystalline, or liquid) of the nitrogen-containing heterocyclic compounds.

Keywords: nitrogen-containing heterocycle, liquid crystal, computer simulation, intermolecular interaction, "structure–property" relationship, translational rigidity

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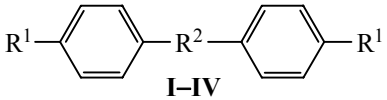
Intermolecular interactions are important factors in many fields of chemistry, physics, and biology; they determine structure of many molecular and supramolecular systems as well as their thermodynamic, kinetic, static, and dynamic properties and the molecules self-assembly and structuring in different aggregate states [1, 2]. Studies of intermolecular interactions of liquid-crystalline compounds are of special importance, since sorbents modified with liquid-crystalline materials are applied for concentrating and isolation of the components from natural (oil) and synthetic mixtures [3, 4].

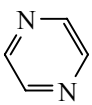
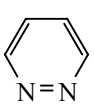
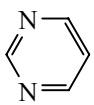
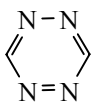
Intermolecular interactions can be studied taking advantage of a variety of theoretical and experimental methods [5] including molecular modeling. Quantum-chemical simulation has become a powerful method to determine structure of isolated molecules and their associates owing to to development of related computer technologies. This allows determination of the intermolecular interactions energy, elucidation of their nature, and revealing the mechanisms of molecules structuring in crystalline, liquid-crystalline, and liquid phases.

Certain structural analogs of 1,4-terphenyl, heterocyclic compounds with the central six-membered nitrogen-containing fragment, are known to exhibit thermotropic smectic and/or nematic liquid-crystalline properties [6] (Scheme 1).

Scheme 1.



I–IV

R^1 = Bu, R^2 =  (**II**),  (**IV**),  (**III**),  (**I**).

Taking advantage of SARD (Structure Activity Relationship & Design) system [7], we have earlier analyzed the relationship between structure and liquid-crystalline properties of compounds **I–IV** and proposed the model for prediction of liquid-crystalline properties [8]. It has been shown that the presence of tetrazine, pyrazine, pyrimidine, or pyridazine fragments in the molecules favors the smectic and nematic properties [9]. Even though the mentioned method allows selection of potentially active liquid-crystalline substances basing of the structural parameters, it cannot be used to determine the energetic factors enhancing the mesomorphism. Quantum-chemical computer simulation of compounds **I–IV** has been used to study the isolated molecules [10], investigate the substituents effect on structural and energetic parameters, and reveal the correlation between the molecules three-ring fragment planarity and the substances melting points, thus estimating the lower limit of the mesophase existence temperature range [11]. However, no correlations involving other liquid-crystalline properties have been found.

Among other data obtained, computer simulation of phases forming molecular associates (the common case of heteroaromatic compounds) allows investigation of intermolecular interactions [12]. In view of the above, we performed quantum-chemical simulation of the interaction energy and molecular ordering of butyl-substituted dimers: 3,6-bis(4-butylphenyl)-1,2,4,5-tetrazine (**I**), 2,5-bis(4-butylphenyl)pyrazine (**II**), 2,5-bis(4-butylphenyl)pyrimidine (**III**) and 3,6-bis(4-butylphenyl)pyridazine (**IV**) taking advantage of the approach based on dynamics of dimers molecular movement at a range of temperaure [13–16]. The reasons for the different liquid-crystalline properties of compounds **I–IV** could be then rationalized by comparison of the translational rigidity coefficients, reflecting the ability of free movement of the molecules in dimers.

Quantum-chemical simulation of the intermolecular interaction energy E_{int} were performed for equilibrium configurations of the dimers located in different layers of the liquid crystal (stacking, St) or in the same layer [planar (Pl) and terminal (T)] via the RHF/6-31G(d,p) (PC GAMESS v.7.1.F) method [17]. The dispersion term was accounted for as described in Ref. [18] using the QChemistry Utility software [19]. The derived energies E_{int} were used as the input data for computing the population of a given configuration with the energy $E_{int} = \varepsilon_i$ with respect to all possible configurations of dimers via the Maxwell–Boltzmann equation:

$$P = \exp(-\beta\varepsilon_i)/\sum_i \exp(-\beta\varepsilon_i),$$

with P, relative probability for the given configuration; $\beta = 1/kT$; k, the Boltzmann constant; T, absolute temperature; ε_i, energy of the ith configuration referenced to the lowest one.

The possibility of free movement of the molecules in the dimer was estimated as follows. The most probable (equilibrium) configuration (mathematical expectation of the value of the displacement) was calculated as the first statistical moment [20]:

$$M_1 = \int_{X_0}^{X_k} X \cdot P(X) \cdot dX / \int_{X_0}^{X_k} P(X) dX,$$

with M_1, the first statistical moment; X, displacement of the molecules in the dimer along the longer axis of the molecule; $P(X)$, relative probability (population) of the given dimer configuration.

Dispersion of the displacements was calculated as the second centered statistical moment:

$$\mu_2 = \int_{X_0}^{X_k} (X - M_1)^2 \cdot P(X) \cdot dX / \int_{X_0}^{X_k} P(X) dX.$$

The reciprocal of μ_2 reflected the translational rigidity of the system. According to the simulation, T-interactions in the dimers of molecules **I–IV** were rather weak as compared to those the St- and Pl-interactions since the relative probability of formation of the former configuration did not exceed 5%.

The nematic character of liquid crystal is often caused by possibility of translational movement along the long axes of the molecules (Fig. 1) [21].

The effect of the dimeric molecules displacement on the relative probability P was determined at T = 300, 445 and 500 K, corresponding to different phases of compounds **I–IV**: crystalline (C), smectic (S), nematic (N), and isotropic liquid **I** (Fig. 1).

Analysis of the probability P (%) changes with moving molecules of compounds **I–IV** along the longer axis of the dimer (ΔX, Å) revealed three characteristic regions (Fig. 2). Regions *1* and *3* corresponded to relatively weak intermolecular interactions; hence, the structurization was insufficient and the liquid-crystalline phase was not formed. Region *2* corresponded

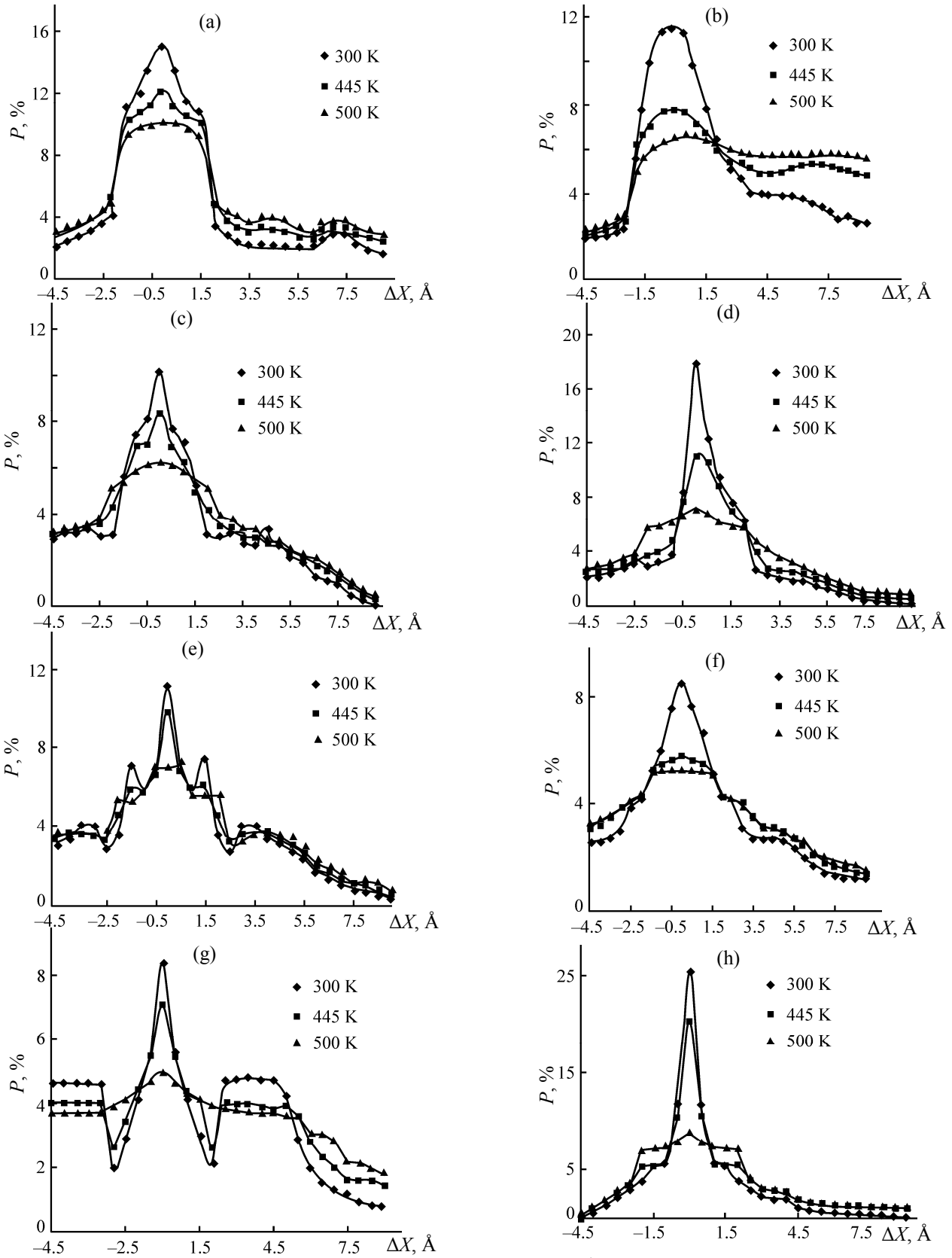


Fig. 1. Probability P (%) as function of the displacement along X axis (ΔX, Å) for (*a*) St and (*b*) Pl interactions in dimers of molecules **I–IV** (T = 300, 445, and 500 K).

to much stronger intermolecular interactions, pointing at the possibility of exhibiting mesomorphic or crystalline properties. The presence of a clearly seen peak in region *2* of the curve was indicative of a well ordered structure and the possibility of formation of the crystalline phase. The gentle sloping observed in region *2* suggested the higher molecular mobility possibly assigned to the presence of liquid crystalline phase.

It has been earlier reported that at T = 300 K compounds **I–IV** are crystalline; at T = 445 K their phase behavior is different: compound **I** is being transformed from nematic state into liquid phase, compounds **II** and **III** form nematic and smectic phases, respectively, and compound **IV** is crystalline; at T = 500 K all the compounds form isotropic liquids (see table) [6].

It was found that the rigidity coefficient $1/\mu_2$ of the St- and Pl-configurations of the dimers decreased with heating. Variation of $1/\mu_2$ values for the St-configuration of the dimers at T = 300 K was typical of the crystalline phase, and its change in the 0.13 (**III**) < 0.14 (**II**) < 0.15 (**I**) < 0.18 Å^{-2} (**IV**) series coincided with the melting points of the substances: 391 (**III**) < 434 (**II**) < 443 (**I**) < 480 K (**IV**).

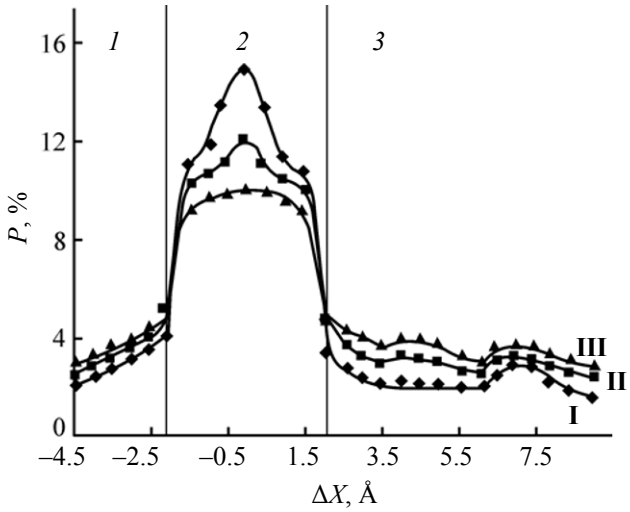


Fig. 2. Characteristic regions in the plots of probability P (%) as function of the displacement along X axis (ΔX, Å) for the dimers of molecules **I–III.**

Hence, the increase of the system translational rigidity caused by the enhanced intermolecular interactions of the molecules located in the different layers of the crystal was reflected in the increase of the melting points (i.e., higher ordering of the crystalline phase). However, such correlation was lacking in the

Values of equilibrium configurations M_1, Å and translational rigidity $1/\mu_2$, Å^{-2} of the dimers and thermal characteristics of phases T and ΔT, K for compounds **I–IV**[a]

Comp. no.	T	St		Pl		mp	T_S	T_N	T_I	ΔT_S	ΔT_N	ΔT	Phase
		M_1	$1/\mu_2$	M_1	$1/\mu_2$								
I	300	1.3	0.15	1.4	0.09	443	–	443	445	–	2	2	C
	445	2.0	0.11	1.8	0.08								N → I
	500	2.4	0.09	2.0	0.07								I
II	300	0.7	0.14	0.5	0.14	434	434	439	455	5	16	21	C
	445	0.8	0.12	0.7	0.12								N
	500	0.9	0.08	0.7	0.07								I
III	300	0.6	0.13	0.7	0.15	391	391	–	459	68	–	68	C
	445	0.8	0.13	1.0	0.14								S
	500	1.2	0.09	1.3	0.07								I
IV	300	1.0	0.18	0.3	0.18	480	480	486	493	6	7	13	C
	445	1.4	0.17	0.5	0.16								C
	500	1.6	0.08	0.9	0.05								I

[a] T, absolute corresponding to the simulation conditions; M_1, equilibrium configuration; $1/\mu_2$, translational rigidity; C, S, N, and I, the phase existing at the corresponding temperature (the arrow denotes the ongoing transition): C, crystalline; S, smectic; N, nematic; and I, isotropic state; mp, melting point; T_S, temperature of transition into smectic phase; T_N, temperature of transition into nematic phase; T_I, temperature of transition from mesophase to isotropic liquid; ΔT_S, temperature range of existence of smectic mesophase; ΔT_N, temperature range of existence of nematic mesophase; ΔT temperature range of existence of mesophase.

case of the Pl-configuration of the dimers: 0.09 (**I**) < 0.14 (**III**) ≈ 0.14 (**II**) < 0.18 Å^{-2} (**IV**).

Hereafter rigidity of the studied systems at 445 K will be covered in detail in order to determine the influence of the central fragment nature on the ability of studied compounds to exhibit liquid-crystalline properties.

For compound **I**, the rigidity $1/\mu_2$ (St) = 0.11 Å^{-2} and $1/\mu_2$ (Pl) = 0.08 Å^{-2} was smaller than that of compounds **II–IV**. This is suggestive that compound **I** exists within the limits of rather weak ordering characteristic of liquid phase. The $1/\mu_2$ (St) value was larger than $1/\mu_2$ (Pl), typical of nematic compounds [13]. Indeed, compound **I** demonstrated nematic properties over a narrow range of mesomorphism ΔT_N = 2 K (see table).

The rigidity values for compound **II** were of $1/\mu_2$ (St) = $1/\mu_2$ (Pl) = 0.12 Å^{-2}, indicative of the enhanced in- and interlayer molecular ordering of compound **II** as compared to compound **I**. On the other hand, equal rigidity of the St and Pl dimer configurations suggested the possibility of the nematic phase existence [14]. Therefore, for compound **II** was expected to exhibit nematic properties over a wider temperature range, conforming with the experimental data ΔT_N = 16 K (see table).

In the case of compound **III**, the rigidity values were of $1/\mu_2$ (St) = 0.13 Å^{-2} and $1/\mu_2$ (Pl) = 0.14 Å^{-2}. Since $1/\mu_2$ (St) < $1/\mu_2$ (Pl), the in-layer interactions of the molecules were stronger than the interlayer ones. The $1/\mu_2$ values for compound **III** were larger than those for compound **II**. Hence, molecular ordering in dimers of compound **III** was enhanced [15], allowing for appearance of smectic properties. The conclusion was confirmed experimentally: compound **III** was a smectic liquid crystal exhibiting a wide temperature range of mesomorphism ΔT_S = 68 K (see table).

Compound **IV** showed by the largest rigidity values of all the studied systems: $1/\mu_2$ (St) = 0.17 Å^{-2} and $1/\mu_2$ (Pl) = 0.16 Å^{-2}. The enhanced ordering resulted in the existence of that compound in the crystalline phase. When the temperature was increased to T = 500 K, the rigidity value decreased to $1/\mu_2$ = 0.05–0.08 Å^{-2}, indicating that the molecules could move freely along the long axis of the molecule, probably leading to the transition into the liquid phase.

Thus, the central heterocyclic fragment of compounds **I–IV** affected the liquid-crystalline properties at T = 445 K in the following way: when $1/\mu_2$ (St) ≥ $1/\mu_2$ (Pl), N-mesophase was formed, and the S-mesophase existed when $1/\mu_2$ (St) < $1/\mu_2$ (Pl). Moreover, the value of the rigidity coefficient $1/\mu_2$ quantitatively characterized the type of the phase formed by compounds **I–IV**: with $1/\mu_2$ (St) > 0.13 Å^{-2} and $1/\mu_2$ (Pl) > 0.14 Å^{-2}, the compound existed in the crystalline phase; with 0.12 < $1/\mu_2$ (St) ≤ 0.13 Å^{-2} and 0.12 < $1/\mu_2$ (Pl) ≤ 0.14 Å^{-2}, the transition to S-mesophase was possible; with 0.11 < $1/\mu_2$ (St) ≤ 0.12 Å^{-2} and 0.08 < $1/\mu_2$ (Pl) ≤ 0.12 Å^{-2}, the transition to N-mesophase was possible; and with $1/\mu_2$ (St) < 0.10 Å^{-2} and $1/\mu_2$ (Pl) ≤ 0.08 Å^{-2}, the compound existed in the liquid phase.

The described trend was not held in the only case: compound **I** was crystalline at $1/\mu_2$ (Pl) = 0.09 Å^{-2}.

In summary, the computer simulation study demonstrated that the translational rigidity coefficients reflecting the ability of the dimerized molecules towards free movement could be used to elucidate the correlation of the compounds chemical structure and the exhibited phase behavior.

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