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Full Articles

"*ortho*-Effect" in thermal Curtius rearrangement of alkylbenzoyl azides into isocyanates: a quantitative interpretation

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The reasons for abnormally high reactivity of *ortho*-alkylbenzoyl azides in thermal Curtius rearrangement were established by the density functional method (PBE/TZ2P approximation). The key factor responsible for the rearrangement rate is the destabilization of the conjugated structure of arylacyl azide through steric effects of the *ortho*-substituents. Additional intramolecular hydrogen bonding, as in *o*-hydroxybenzoyl azide molecule, stabilizes the conjugated structure and increases the energy barrier to the reaction. Quantitative interpretation of the "*ortho*-effect" is given based on the dependence of the reactivity of *ortho*-alkylbenzoyl azides on the dihedral angle, which characterizes the extent of coplanarity of the acyl azide group and benzene ring.

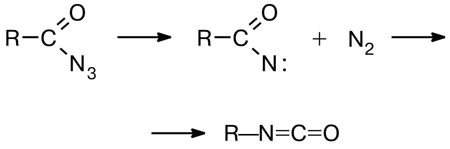
Key words: acyl azides, thermal Curtius rearrangement, quantum-chemical calculations, "*ortho*-effect", reaction mechanism.

The thermal Curtius rearrangement of acyl azides is one of a few phosgene-free methods of synthesis of isocyanates. The mechanism of this reaction has long been a moot question.[1] It was assumed that the process can proceed either in one stage (Scheme 1), when the breakdown of the acyl azide group, formation of isocyanate, and liberation of a nitrogen molecule occur in a concerted fashion, or in several stages (Scheme 2) involving decomposition of acyl azide to a carbonylnitrene biradical followed by monomolecular rearrangement of the latter into isocyanate.

Scheme 1

$$\mathrm{R{-}C(O){-}N_3 \longrightarrow R{-}N{=}C{=}O + N_2}$$

Scheme 2



$$\mathrm{R{-}C({=}O){-}N_3 \longrightarrow R{-}C({=}O){-}\ddot{N} + N_2 \longrightarrow R{-}N{=}C{=}O}$$

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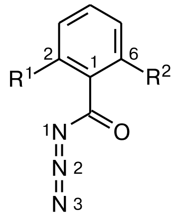
The idea of the stepwise reaction mechanism is based on the analogy with the photochemical rearrangement of acyl azides (in this case, the formation of nitrenes is undoubtful).[2] For instance, both singlet and triplet acylnitrenes formed in the photochemical decomposition of acyl azides were repeatedly identified based on the products of their reactions with radical traps[3] and by IR and UV spectroscopy in low-temperature matrices.[4] However, studies of thermal decomposition of alkyl- or arylacyl azides by different methods (from the rate of nitrogen liberation, consumption of the initial acyl azide, or accumulation of the final isocyanate) never revealed the formation of acylnitrenes or any anomalies of the reaction kinetics.[1]

The mechanism of thermal Curtius rearrangement was established recently[5,6] in quantum-chemical studies of the structure of acyl azides and fragments of the potential energy surface (PES) of the reaction using different-level computational schemes. It was found that acyl azides $RC(O)N_3$ can exist as *syn*- and *anti*-conformers relative to the C—N bond; as a consequence, their rearrangement into isocyanates occurs under conformational control. The *syn*-conformers are more stable then corresponding *anti*-conformers and rearrange in a concerted fashion (see Scheme 1). In this case the activation energy is much lower than that of the rearrangement of the *anti*-conformers involving the formation of acylnitrenes as reaction intermediates (see Scheme 2). The results of calculations[5] suggest that acylnitrenes can form only in the thermolysis of alkoxyacyl azides, because here the *anti*-conformers are more stable than the corresponding *syn*-conformers and transformation into isocyanates requires a lower activation barrier. Indeed, only thermolysis of ethoxycarbonyl azide resulted in the corresponding acylnitrene that was experimentally detected by the CIDNP technique.[7]

Advances in quantum-chemical studies of the structure of acyl azides and the PESs of their thermal rearrangements into isocyanates gave us an impetus to solving some other problems concerned with the mechanism of this reaction including the reasons for anomalous reactivity of *ortho*-substituted benzoyl azide derivatives in the Curtius rearrangement. A feature of the kinetics of thermal rearrangement of arylacyl azides is low sensitivity of the reaction rate to the structures of the *meta*- and *para*-substituted benzoyl azide derivatives.[8,9] For instance, the rate constant for the reaction shows a less than twofold decrease on going from the *m*-methyl- to *m*-nitro-substituted benzoyl azide derivatives provided that the Hammett σ-constants of the corresponding substituents change by an order of magnitude from –0.07 to +0.71. At the same time the rate constants for thermal decomposition of *ortho*-alkylbenzoyl azides are 1.5—2 orders of magnitude higher than those for the reactions involving benzoyl azide and its *meta*- and *para*-substituted derivatives.[10] Here, it seems to be quite natural to use the hypothesis of the so-called "*ortho*-effect" in organic chemistry,[11] or violation of coplanarity of the system under the action of substituent (bulky *ortho*-substituents cause the fragment involved in the reaction to deviate from the plane and thus to violate its resonance conjugation with the benzene nucleus). This hypothesis is, in particular, in qualitative agreement with the data on abrupt decrease in the reactivity of *o*-hydroxybenzoyl azide[10] in which an intramolecular hydrogen bond between the OH and CON_3 groups stabilizes the planar structure of $HO—Ar—C(O)N_3$.

This work is devoted to establishment and substantiation of the reasons for high reactivity of *ortho*-alkylbenzoyl azides in thermal Curtius rearrangement by quantum chemistry methods. To this end, we studied the structures of acyl azides **1—6** and calculated fragments of the PES of isomerization and concerted rearrangement of *syn*-conformers into corresponding isocyanates.



1—6

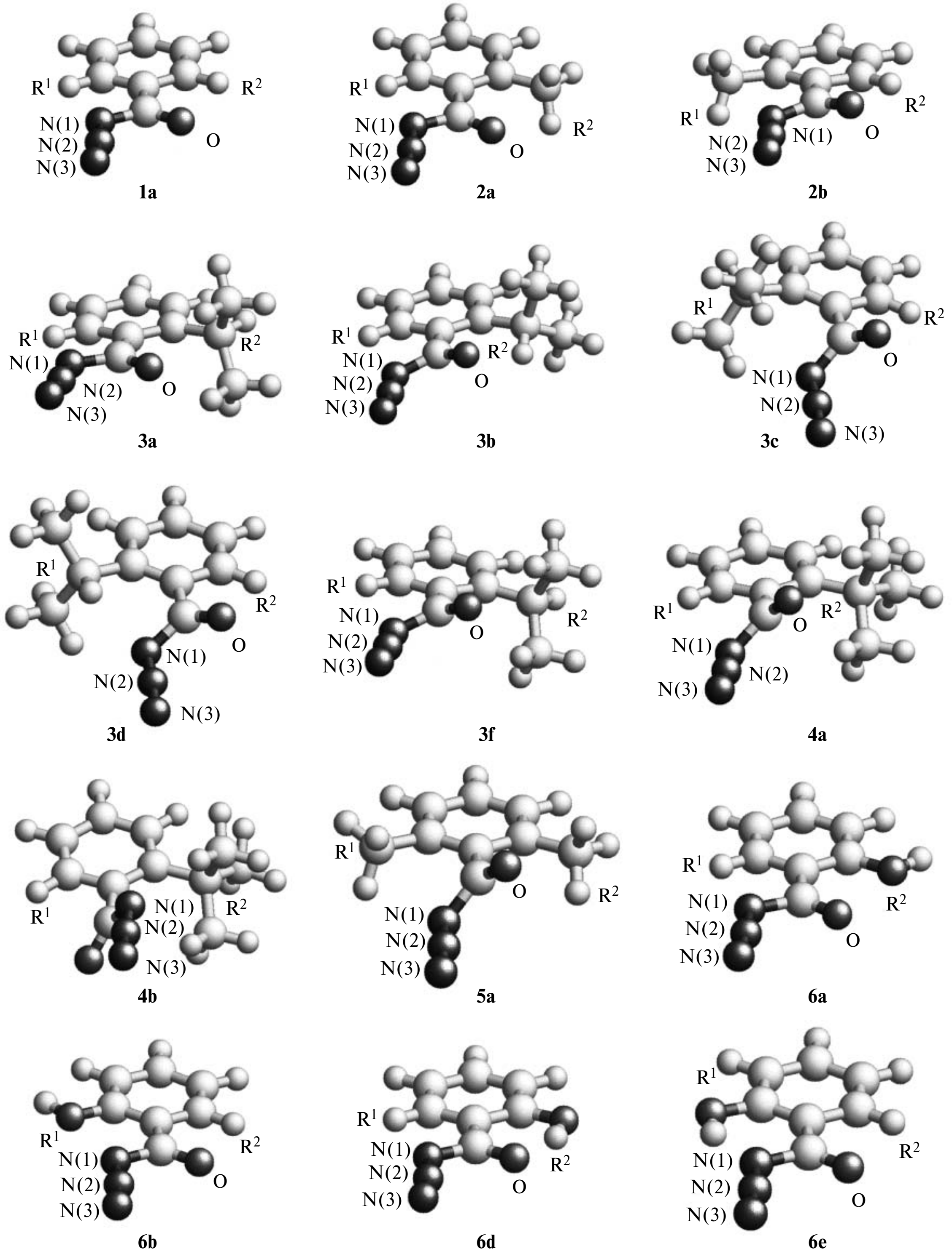
R^1 = H (**1—4**, **6**), Me (**5**)
R^2 = H (**1**), Me (**2**, **5**), Pr^i (**3**), Bu^t (**4**), OH (**6**)

Calculation Procedure

Calculations were carried out by the density functional theory (DFT) using the nonempirically generalized gradient approximation and the PBE functional[12,13] implemented in the PRIRODA program.[14] One-electron wave functions were expanded using the TZ2P extended atomic basis sets of contracted Gaussian functions of the types {311/1} for the H atom and {611111/411/11} for the C, N, and O atoms. Geometry optimization was performed for all stable compounds and transition states. The characters of the stationary points located (minimum or saddle point) were determined by calculating the eigenvalues of the matrix of the second derivatives of energy with respect to the coordinates of atomic nuclei. Correspondence between transition states and a given transformation was established by the IRC method. All the energies reported in this work refer to T = 0 K; the zero-point energy correction was not applied. Preliminarily, we have found that this correction is very small and has virtually no effect on the relative changes in the energy of the systems under study.

Results and Discussion

Isomerization and relative stabilities of *syn*- and *anti*-conformers of arylacyl azides. The possibility for acyl azides to exist as a mixture of *syn*- and *anti*-conformers[5,6] was confirmed in this work by calculations of the structures of the compounds under study. Figures 1 and 2 show the structures and Table 1 lists the energy characteristics of the *syn*- and *anti*-conformers of *ortho*-substituted arylacyl azides **1**—**6**. The compounds can form different numbers of conformers depending on the substituent. The number of the *syn*- and *anti*-conformers is equal for molecules **1**, **2**, and **5** (one, two, and one, respectively) and different for molecules **3**, **4**, **6**. The largest number of the *syn*-conformers (five) was found for molecule **3**,



1a **2a** **2b**

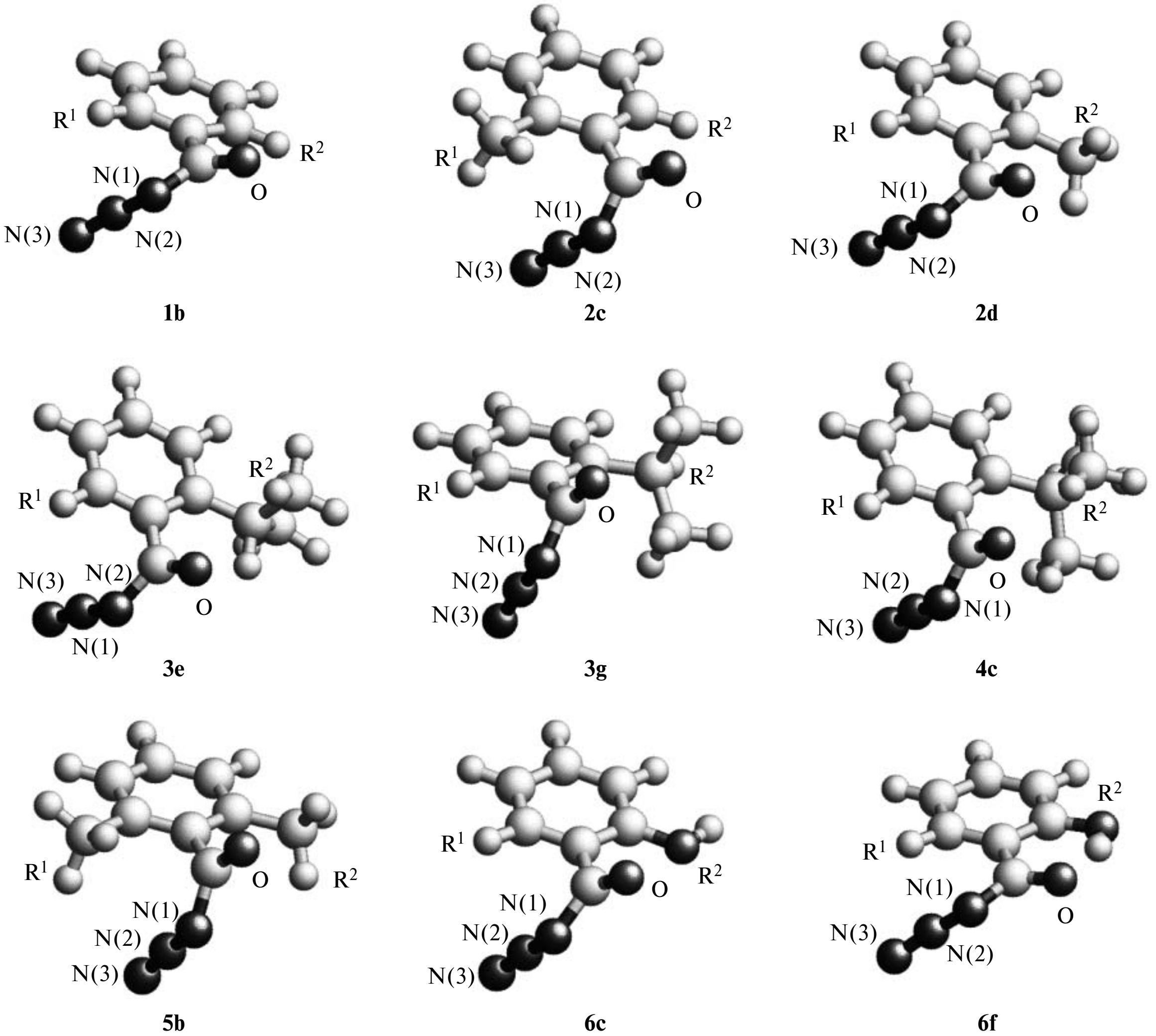
3a **3b** **3c**

3d **3f** **4a**

4b **5a** **6a**

6b **6d** **6e**

Fig. 1. *syn*-Conformers of arylacyl azides **1**—**6**.



1b **2c** **2d**

3e **3g** **4c**

5b **6c** **6f**

Fig. 2. *anti*-Conformers of arylacyl azides **1**—**6**.

which has only two *anti*-conformers. *o*-Hydroxybenzoyl azide **6** has four *syn*- and only two *anti*-conformers. *o*-*tert*-Butylbenzoyl azide **4** has two *syn*-conformers and only one *anti*-conformer. It should be noted that usually the relative stabilities of different *syn*-conformers of the same acyl azide molecule differ insignificantly (by 2—5 kcal mol^{-1}). Among the *syn*-conformers shown in Fig. 1, the most stable are **1a**, **2a**, **3b**, **4a**, **5a**, and **6d** (see Table 1). Calculations of particular *syn*-conformers showed that interconversions of the conformers of identical chemical composition require the overcoming of energy barriers a few kilocalories per mole high. Because of this they exist as rather stable structures. The activation energies of the direct and reverse rearrangements are listed in Table 2.

The data in Table 1 show that the *syn*-conformers are more stable than the corresponding *anti*-conformers. The electronic energy difference between the most stable *syn*- and *anti*-conformers is 3—7 kcal mol^{-1}, except for molecule **6** (7.5—18.0 kcal mol^{-1} depending on the mutual arrangement of the N or O atoms of the acyl azide group with respect to the OH group in the substituent) due to additional stabilization of planar *syn*-structure through intramolecular hydrogen bond. For the same reason the stabilities of different *syn*-conformers of molecule **6** differ appreciably (*e.g.*, conformer **6d** is nearly 13 kcal mol^{-1} more stable than conformer **6b**).

A typical PES profile of the *syn*—*anti*-isomerization of arylacyl azides is shown in Fig. 3 taking compounds **1**—**3** and **5** as examples; more detailed data on the energy barriers separating the corresponding conformers are listed in Table 3. The activation energies for the *syn*—*anti*-isomerization of acyl azides **1**—**6** are very similar (8.4—9.3 kcal mol^{-1}), being somewhat lower for the reverse reaction (1.8—6.0 kcal mol^{-1}). In this respect the *syn*—*anti*-isomerization of arylacyl azides obeys the same pattern as that established[6] for the model compounds $HC(O)N_3$ and $MeC(O)N_3$.

Table 1. Energy characteristics of *syn*- and *anti*-conformers of *ortho*-substituted benzoyl azide derivatives

Conformer	Conformer type	$-E$/au	ΔE* /kcal mol^{-1}
1a	*syn*	508.79941	0
1b	*anti*	508.78870	6.7
2a	*syn*	548.07316	0
2b	*syn*	548.06960	2.2
2c	*anti*	548.06202	7.0
2d	*anti*	548.06375	5.9
3a	*syn*	626.60875	3.2
3b	*syn*	626.61377	0
3c	*syn*	626.60560	5.1
3d	*syn*	626.61063	2.0
3e	*anti*	626.60610	4.8
3f	*syn*	626.60922	2.9
3g	*anti*	626.60338	6.5
4a	*syn*	665.87540	0
4b	*syn*	665.87234	1.9
4c	*anti*	665.87112	2.7
5a	*syn*	587.34229	0
5b	*anti*	587.33774	2.9
6a	*syn*	583.97792	12.4
6b	*syn*	583.97730	12.8
6c	*anti*	583.96912	17.9
6d	*syn*	583.99772	0
6e	*syn*	583.98948	5.2
6f	*anti*	583.98565	7.6

* All ΔE values for conformers of compounds **1—6** were calculated with respect to the most stable conformers.

Table 3. Activation energies of direct and reverse reactions of *syn—anti*-isomerization of arylacyl azides

syn-Conformer	*anti*-Conformer	E_a/kcal mol^{-1}	
		syn → *anti*	*anti* → *syn*
1a	**1b**	9.2	2.5
2a	**2d**	8.8	2.9
3b	**3e**	8.6	3.8
3f	**3g**	8.6	5.0
4a	**4c**	8.6	5.9
5a	**5b**	8.9	6.0
6a	**6c**	8.4	2.9
6d	**6f**	9.3	1.7

Potential energy surface of the rearrangement of *syn*-conformers into isocyanates and relation between the reactivity and structure of arylacyl azides. The PES profiles for the Curtius rearrangement of the *syn*-conformers of arylacyl azides are shown in Fig. 4. Table 4 lists the electronic energies of the initial reactants, reactions products, and transition states (TS) of the concerted rearrangement of the *syn*-conformers, as well as the activation energies (E_a) and enthalpies (ΔH) of the reactions studied. According to the Polanyi—Semenov relationship, the last two parameters of benzoyl azide derivatives are linearly related, namely, $E_a = 67.3 + 0.84\Delta H$ (correlation coefficient $R^2 = 0.932$). Depending on substituent, the calculated activation energies of the reactions are 4—6 kcal mol^{-1} higher than the experimental values ob-

Table 2. Activation energies of direct and reverse rearrangements of conformers of arylacyl azide molecules

Conformer		E_a/kcal mol^{-1}	
I	II	I → II	II → I
2a	**2b**	5.6	3.4
3a	**3c**	3.5	1.6
3b	**3d**	4.1	2.1
3a	**3d**	6.5	7.7
4a	**4b**	3.0	1.0
6a	**6b**	4.4	4.0
6d	**6e**	17.2	12.0

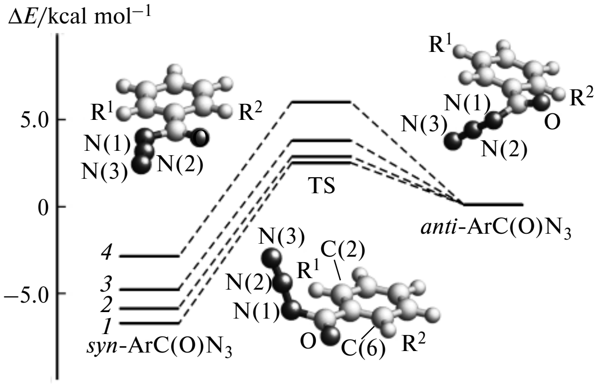


Fig. 3. PES profiles for *syn—anti*-isomerization of arylacyl azides **1a** (*1*), **2a** (*2*), **3b** (*3*), and **5a** (*4*).

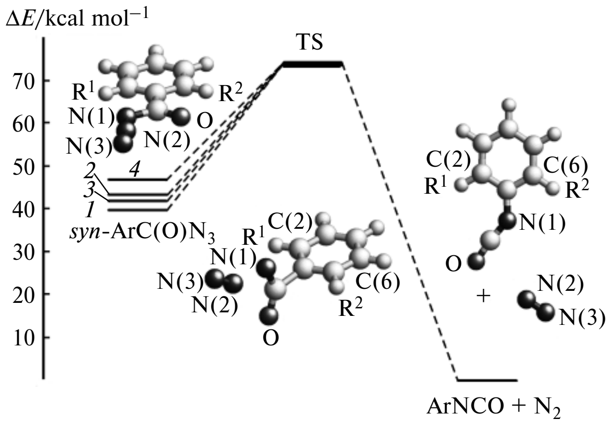


Fig. 4. PES profiles for rearrangements of *syn*-conformers of arylacyl azides **1a** (*1*), **2a** (*2*), **3b** (*3*), **5a** (*4*) into corresponding isocyanates.

Table 4. Electronic energies of the reactants ($RC(O)N_3$), transition states (TS), reaction products ($RNCO + N_2$), activation energies, and enthalpies of rearrangements of *syn*-conformers

syn-Conformer	$-E$/au			E_a	$-\Delta H$
	$RC(O)N_3$	TS	$RNCO + N_2$	kcal mol^{-1}	
1a	508.79941	508.74450	508.86382	34.5	40.4
2a	548.07316	548.02280	548.14102	31.6	42.5
3b	626.61377	626.56601	626.68393	30.0	44.0
4a	665.87540	665.83011	665.95077	28.4	47.3
5a	587.34229	587.30025	587.41805	26.4	47.6
6e	583.98948	583.93520	584.05090	34.1	38.5

tained in studies of thermal rearrangement of the same acyl azides in nitrobenzene.[10] The difference between the theoretical enthalpies of the reactions under study and the experimental ΔH values determined in solution (-47.1 kcal mol^{-1})[15] is also small and quite admissible taking into account the fact that quantum-chemical calculations were carried out for the gas phase. More detailed consideration of the differences between the theoretical and experimental parameters of the reactions under study is given in our previous communication[6] where we also presented the results of PES calculations for stepwise rearrangement of the *anti*-conformers of the model compounds $RC(O)N_3$ proceeding with much higher activation energy compared to the experimentally observed values.

Transformation of the molecular structure of acyl azide upon concerted rearrangement into isocyanate[6] is shown in Fig. 5 taking the *syn*-conformer **1a** as an example. In the transition state the distance between the N(1) and N(2) atoms is 1.712 Å, being much longer than the N(1)—N(2) bond length in the initial acyl azide. The formation of a transition state involves an increase in the interatomic distance O...N(2) and a change in the N(2)—N(3) bond length from 1.138 to 1.112 Å, which approaches the bond length in the nitrogen molecule (1.103 Å). Gradual abstraction of N_2 molecule creates prerequisites to reorganization of the molecular fragment in the transition state in a fashion leading to the final product. It should be noted that the C(2)—C(6)—O—N(1) dihedral angle in the transition state of the concerted Curtius rearrangement is only slightly different from 90° (Table 5). This indicates that the benzene nucleus and the acyl azide group are arranged in perpendicular planes. The relation between the relative reactivity of *ortho*-arylacyl azides $\lg(k/k_0)$ (k and k_0 are the rate constants for the rearrangement of substituted and unsubstituted arylacyl azides, respectively) and the dihedral angle α in the *syn*-conformers is shown in Fig. 6. The correlation was obtained using the α values for all stable conformers (see Table 5), although, strictly speaking, it is unclear whether or nor all of them are involved in the reaction. Despite some scatter of points, which is quite natural with allowance for such a broad variation of the structure, the plot shown in Fig. 6 represents the quantitative interpretation of the "*ortho*-effect". It follows that

Table 5. Dihedral angles C(2)—C(6)—O—N(1) (α) and the R(1)...N(1) N(1)...N(2) distances (d) in the initial *syn*-conformers and in the transition states (TS) of concerted Curtius rearrangement into isocyanates

syn-Conformer	α/deg		d/Å			
			R^1...N(1)		N(1)...N(2)	
	Acyl azide	TS	Acyl azide	TS	Acyl azide	TS
1a	0.2	83.7	2.408	3.076	1.242	1.712
2a	0.1	77.0	2.286	3.393	1.240	1.702
2b	11.9	—	2.794	—	1.243	—
3a	0.3	—	2.201	—	1.240	—
3b	15.1	78.7	2.282	3.416	1.240	1.703
3c	44.9	—	3.233	—	1.245	—
3d	32.9	—	2.960	—	1.244	—
3f	29.2	—	4.503	—	1.244	—
4a	40.2	73.8	2.418	3.734	1.242	1.722
4b	55.3	—	3.389	—	1.245	—
5a	45.4	83.5	2.905	3.249	1.244	1.686
6a	0.2	—	2.294	—	1.239	—
6b	0.1	—	2.638	—	1.242	—
6d	0.0	—	2.418	—	1.244	—
6e	0.0	81.3	2.633	3.186	1.244	1.701

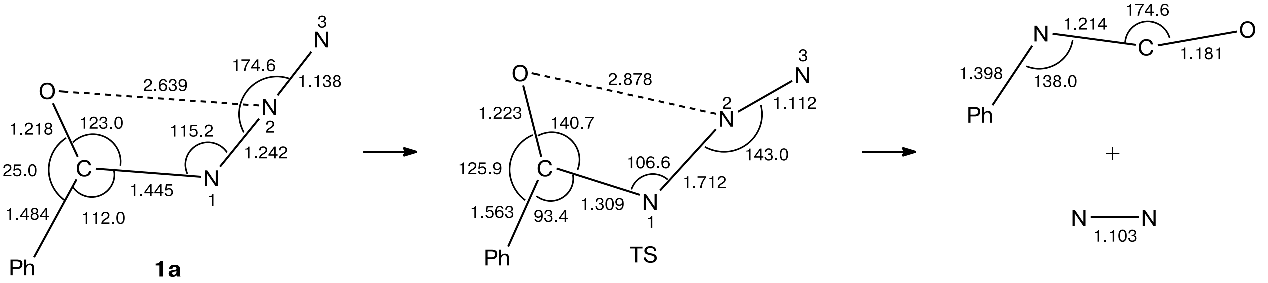


Fig. 5. Molecular geometries of *syn*-conformer **1a**, transition state, and products of thermal Curtius rearrangement; shown are the interatomic distances (Å) and bonding angles (deg).

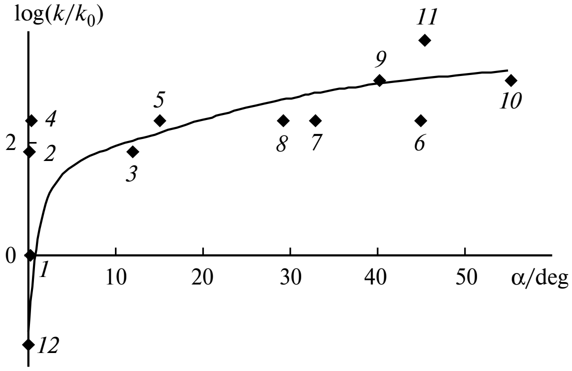


Fig. 6. Reactivity of substituted *ortho*-arylacyl azides **1a** (*1*), **2a** (*2*), **2b** (*3*), **3a** (*4*), **3b** (*5*), **3c** (*6*), **3d** (*7*), **3f** (*8*), **4a** (*9*), **4b** (*10*), **5a** (*11*) and **6a—d** (*12*) plotted *vs*. dihedral angle C(2)—C(6)—O—N(1) in *syn*-conformers (α), which characterizes the deviation of the acyl azide group from the benzene ring plane under the action of the *ortho*-substituent.

the key factor responsible for acceleration of the Curtius rearrangement is the destabilization of the conjugated structure of arylacyl azide due to steric effects of the *ortho*-substituents. Additional intramolecular hydrogen bonding, as in the *ortho*-hydroxybenzoyl molecule **6**, stabilizes the conjugated molecular structure. As a result, the energy barrier increases and the reaction rate decreases.

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