Quantum-Chemical Study on the Reaction of Phenyl Isocyanate with Linear Methanol Associates: II.* Addition at the C=O Bond

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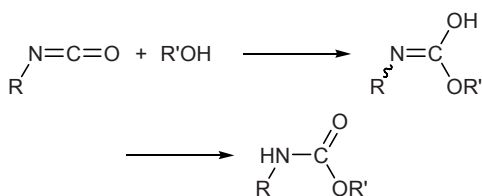*e-mail: samuil@mi.ru*

Abstract—Addition of linear methanol associates at the C=O group of phenyl isocyanate involves a concerted cyclic asymmetric late transition state. The reaction is accompanied by formation of pre- and post-reaction complexes. Isomerization of intermediate methyl hydrogen phenylimidocarbonate into methyl phenylcarbamate is characterized by a considerable energy barrier. The reactivity of methanol molecules increases in parallel with the degree of their association, which is related to increase in their electron-donor power. Comparison of the calculated parameters for the addition of methanol associates at the C=N and C=O bonds of phenyl isocyanate clearly indicates that the first path is preferred.

In the preceding communication we presented the results of our quantum-chemical study on the addition of linear methanol associates at the C=N bond of phenyl isocyanate [1]. We found that these transformations involve concerted asymmetric late transition states and that the energy barriers decrease as the degree of association of methanol molecules increases. A probable reason is increase in the electron-donor power of methanol associates in going from monomeric molecule to dimer and trimer. However, alcohols are capable of adding not only at the C=N bond of isocyanates but also at the C=O bond with intermediate formation of alkyl hydrogen imidocarbonates whose subsequent isomerization should yield the corresponding alkyl carbamates (Scheme 1).

The available kinetic data on reactions of alcohols with isocyanates can be interpreted in terms of addition at both C=N and C=O bond with equal probability. We believe that the only way to distinguish between the above reaction paths is quantum-chemical calculation of the free energy barriers corresponding to these transformations. Comparison of the energy barriers should make it possible to estimate the contribution of each reaction path to the overall reaction rate. In the present article we report the results of our quantum-chemical calculations on the reactions of phenyl isocyanate (**I**) with linear methanol associates **IIa–IIc** at the C=O bond of the former.

The calculations were performed at the B3LYP/6-311++G(df,p) level of theory using Gaussian 03 software package [2, 3]. The geometric parameters of the reactant molecules were preliminarily optimized using Priroda 6 program [4] with the L11 basis set (an analog of cc-pCVDZ [5]). Transition states were localized by the first negative Hessian eigenvalue, and their validity was confirmed by descent from the transition state point to both sides according to the internal reaction coordinate procedure (IRC), followed by optimization of geometric parameters of pre- and post-reac-
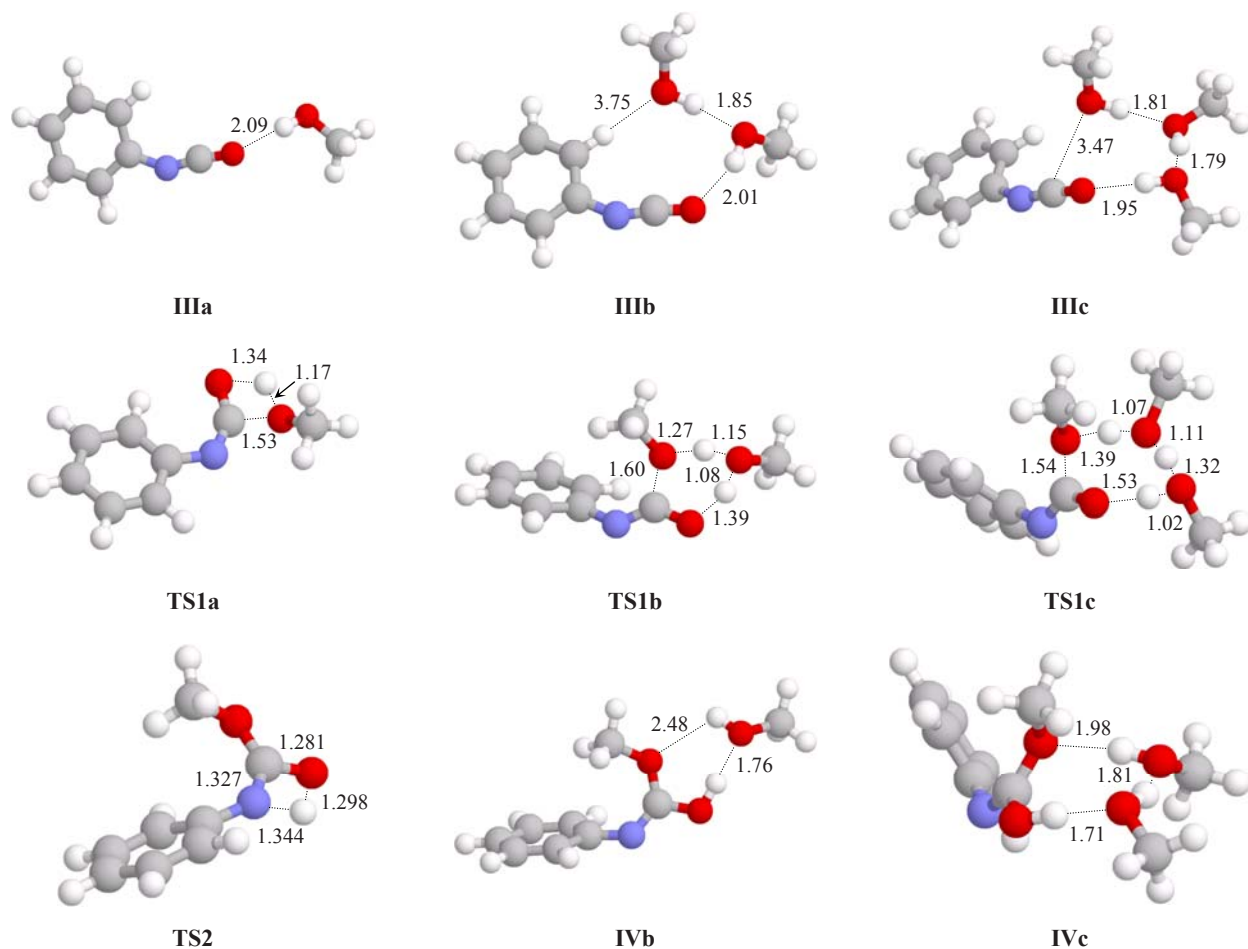
Scheme 1.

* For preceding communication, see [1].

Fig. 1. Ball-and-rod models of pre-reaction complexes **IIIa–IIIc**, transition states **TS1a–TS1c** and **TS2**, and post-reaction complexes **IVb** and **IVc**. Some interatomic distances (Å) are given.

tion complexes thus revealed. The most favorable conformers were determined as described in [1].

The calculations showed that the addition of methanol associates at the carbonyl group of phenyl isocyanate is a complex process involving formation of pre- and post-reaction complexes (Scheme 2). The structures of pre-reaction complexes **IIIa–IIIc**, post-reaction complexes **IVb** and **IVc**, and transition states **TSa–TSc** are shown in Fig. 1, and Table 1 contains the calculated thermodynamic parameters of particular stages. The reactions of isocyanate **I** with methanol associates **IIa–IIc** proceed through pre-reaction complexes **IIIa–IIIc** as intermediates. Their formation is characterized by small negative enthalpies and large negative entropies. The stability of complexes **IIIa–IIIc** increases in parallel with the degree of methanol association. The relative change in the Gibbs energies at the stage of formation of pre-reaction complexes is determined by the change in the enthalpies.

Scheme 2.

PhNCO + (MeOH)$_n$ ⟶ PhNCO · (MeOH)$_n$

I   **IIa–IIc**   **IIIa–IIIc**

n = 1 (**a**), 2 (**b**), 3 (**c**).

IIIa–IIIc ⟶ **TS1a–TS1c**

TS1a ⟶ Ph—N=C(OH)(OMe)
                        IVa

TS1b, TS1c ⟶ Ph—N=C(OH)(OMe) · (MeOH)$_n$
                              IVb, **IVc**

⟶ **IVa** + **IIa, IIb**

n = 1 (**b**), 2 (**c**).

IVa ⟶ **TS2** ⟶ PhNHCOOMe
                                V

Table 1. Variation of the Gibbs energy (ΔG), enthalpy (ΔH), and entropy (ΔS) in particular stages of the reaction of phenyl isocyanate (**I**) with linear methanol associates **IIa**–**IIc** in the gas phase at 298 K

Reaction	ΔG, kJ/mol	ΔH, kJ/mol	ΔS, J mol^{-1} K^{-1}
I + IIa → IIIa	22.6	–8.2	–103.6
IIIa → TS1a	200.3	179.6	–72.2
TS1a → IVa	–163.4	–162.1	0.5
I + IIb → IIIb	20.0	–20.8	–137.0
IIIb → TS1b	152.4	124.5	–93.6
TS1b → IVb	–83.2	–74.0	30.8
IVb → IVa + IIa	–39.4	–3.0	122.1
I + IIc → IIIc	15.6	–23.0	–130.9
IIIc → TS1c	144.8	111.3	–112.4
TS1c → IVc	–73.0	–63.3	32.4
IVc → IVa + IIb	–40.4	10.5	170.7
IVa → TS2	141.1	138.8	–4.0
TS2 → V	–225.0	–223.3	5.1

We showed previously that pre-reaction complexes (having a different structure than those discussed in the present article) are also formed in the addition of methanol associates at the C=N bond of phenyl isocyanate [1]. Their stability was found to decrease as the degree of methanol association increased, and the relative variation in the corresponding Gibbs energies depended mainly on the change in the entropy. Pre-reaction complexes **IIIa**–**IIIc** in the addition of methanol associates **IIa**–**IIc** at the C=O bond of phenyl isocyanate (**I**) turned out to be more stable than in the addition at the C=N bond [1].

Figure 1 shows that the addition involves concerted cyclic transition states in which rupture of old bonds and formation of new bonds occur simultaneously. Table 2 contains the calculated activation parameters for the reactions of isocyanate **I** with associates **IIa**–**IIc**. The corresponding data for the addition at the

C=N bond [1] are also given for comparison. It is seen that the addition at both C=N and C=O bonds is characterized by large negative entropies of activation. The entropies of activation for the reactions of particular methanol associates with isocyanate **I** at the C=N and C=O bonds differ only slightly. On the other hand, the Gibbs energy barrier in the addition at the C=O bond is considerably higher. The main reason is that the enthalpy of activation in the addition at the C=O bond is larger than in the addition at the C=N bond. In both cases, the difference in the Gibbs energies of activation is determined by the difference in the enthalpies of activation. The enthalpies and entropies of activation for the two processes give rise to isokinetic relationship. The reaction at the carbonyl group conforms to Eq. (1).

$$\Delta H^{\neq} \text{ (J/mol)} = 388\,028 + 1232\,\Delta S^{\neq}; \ R = 0.999. \qquad (1)$$

The transformation involving the C=N bond conforms to Eq. (2) [1]:

$$\Delta H^{\neq} \text{ (J/mol)} = 461\,392 + 1715\,\Delta S^{\neq}; \ R = 0.999. \qquad (2)$$

Both reaction paths display the same tendency: the Gibbs energy (enthalpy) barrier decreases as the degree of methanol association increases, i.e., in going from $n = 1$ (**IIa**) to $n = 3$ (**IIc**). As we already noted, the ionization potentials of associates **IIa**–**IIc** decrease in the same order. Thus variation of the activation parameters in each case is consistent with nucleophilic character of the process.

Comparison of the Gibbs energies and enthalpies of activation in the addition of methanol associates **IIa**–**IIc** at the C=N and C=O bonds of **I** suggests higher sensitivity of the former process to structural variations of alcohol associates. The calculated Gibbs energies and enthalpies of activation in the above reactions are interrelated through Eqs. (3) and (4).

$$\Delta G^{\neq}_{C=N} = -49.5 + 1.02\,\Delta G^{\neq}_{C=O}; \ R = 0.997; \qquad (3)$$
$$\Delta H^{\neq}_{C=N} = -49.3 + 1.02\,\Delta H^{\neq}_{C=O}; \ R = 0.997. \qquad (4)$$

Table 2. Gibbs energies ($\Delta G^{\neq}$), enthalpies ($\Delta H^{\neq}$), and entropies ($\Delta S^{\neq}$) of activation in the addition of linear methanol associates **IIa**–**IIc** at the C=N and C=O bonds of phenyl isocyanate (**I**) in the gas phase at 298 K

Reaction	Addition at the C=N bond [1]			Addition at the C=O bond		
	$\Delta G^{\neq}$, kJ/mol	$\Delta H^{\neq}$, kJ/mol	$\Delta S^{\neq}$, J mol^{-1} K^{-1}	$\Delta G^{\neq}$, kJ/mol	$\Delta H^{\neq}$, kJ/mol	$\Delta S^{\neq}$, J mol^{-1} K^{-1}
I + IIa	179.2	127.1	–174.8	222.9	171.4	–175.8
I + IIb	124.1	53.5	–236.3	172.4	103.7	–230.6
I + IIc	117.0	44.1	–244.4	160.4	88.3	–243.3

Thus the reactions at the C=N bond of isocyanate **I** are more sensitive to structural variations of methanol associates **IIa–IIc** and are characterized by a lower energy barrier, as compared to the reactions involving the C=O bond; i.e., anomalous selectivity is typical of these transformations. The concept of anomalous selectivity was considered in detail in [6, 7]. It appears when the relative reactivity of a series of compounds toward two different substrates is determined by differences in orbital donor–acceptor interactions, which can be estimated on a quantitative level through the stabilization energy. The latter depends on the energies of interacting molecular orbitals (MO) and coefficients of the corresponding atomic orbitals in these MOs [8, 9].

The reaction of isocyanates with alcohols may be regarded as nucleophilic addition at multiple bonds. In these processes, interaction between the highest occupied molecular orbital (HOMO) of nucleophile and the lowest unoccupied molecular orbital (LUMO) of electrophile *a priori* predominates over interaction between the other couple of frontier MOs [10]. Figure 2 shows the structures of the second unoccupied MO of isocyanate **I** and HOMOs of methanol associates **IIa–IIc**. The LUMO of isocyanate **I** is localized on the aromatic ring, so that it cannot be responsible for the reaction under study. It may be seen from Fig. 2 that stabilizing interactions in the addition of methanol

associates **IIa–IIc** at the C=N bond of isocyanate **I** are interactions between the oxygen atom in the alcohol, on the one hand, and carbon and nitrogen atoms of phenyl isocyanate, on the other. The stabilizing factor in the reaction at the C=O bond is interaction between the oxygen atom in the alcohol and the carbon atom of the isocyanato group, while interaction between the former and the oxygen atom in the isocyanate is destabilizing. Therefore, the stabilization energy in the addition at the carbonyl group should always be smaller than in the addition at the C=N group. The stabilization energies in the addition of a series of methanol associates at the C=O and C=N bonds should be linearly related since the relative reactivity of methanol associates is determined by the same factor, their electron-donor power (the calculated vertical ionization potentials of monomeric methanol, dimer, and trimer are 10.34, 8.82, and 8.12 eV, respectively). Thus the above differences in the interactions between frontier molecular orbitals in the addition of methanol associates **IIa–IIc** at the C=O and C=N bonds of isocyanate **I** are responsible for the observed anomalous selectivity.

In order to estimate quantitatively the degree of rupture of old bonds and formation of new bonds in transition states **TS1a–TS1c** we introduced a special parameter *f*. The parameter *f* for formation of new bonds was defined according to Eq. (5):
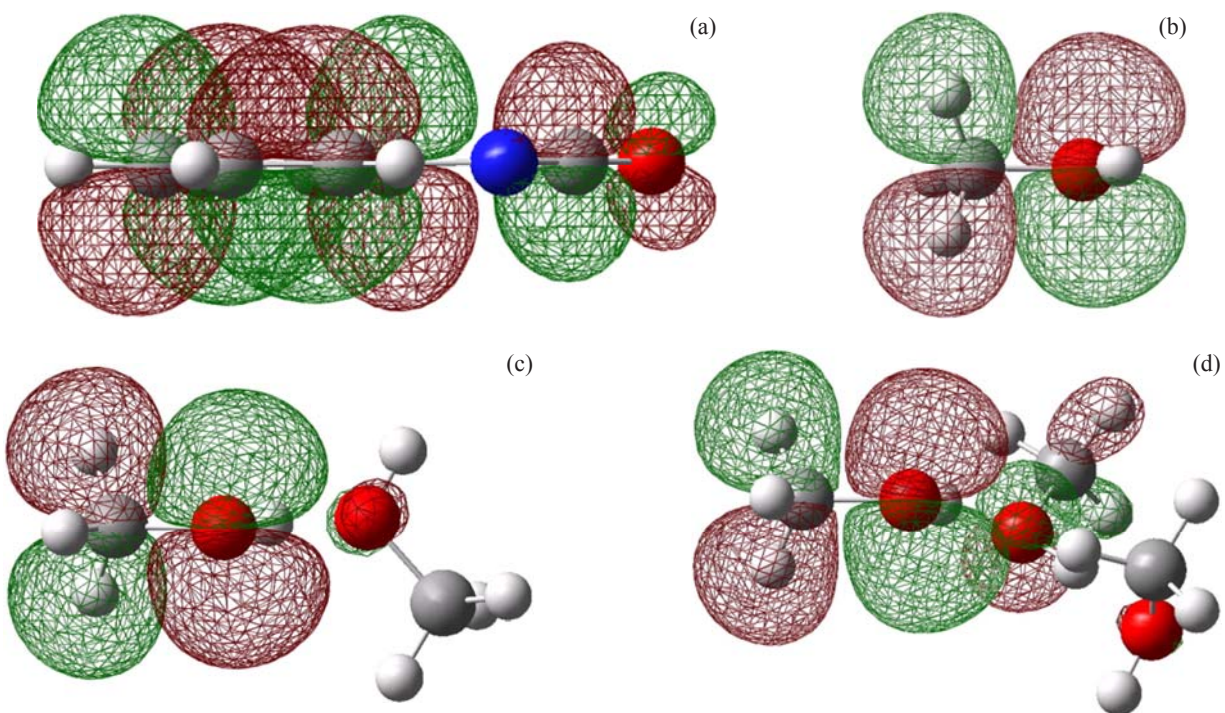

Fig. 2. Structures of (a) second unoccupied molecular orbital of phenyl isocyanate and highest occupied molecular orbitals of (b) methanol monomer, (c) dimer, and (d) trimer.

$$f_{new}\ (\%) = d_{pr}/d_{TS} \times 100, \qquad (5)$$

where d_{pr} is the length of a bond in the product, and d_{TS} is the length of the same bond in the transition state. The degree of rupture of old bonds was defined as the difference between the bond lengths in the transition state and in the initial compound divided by the difference between the bond lengths in the product and in the initial compound:

$$f_{old}\ (\%) = (d_{TS} - d_0)/(d_{pr} - d_0) \times 100. \qquad (6)$$

Table 3 contains the calculated values of f_{new} and f_{old} for different bonds (both newly forming and old) in transition states **TS1a–TS1c**. These data indicate that transition states **TS1a–TS1c** are characterized by high degrees of both rupture of old bonds and formation of new bonds, i.e., the transition states in the reactions under study are late. Furthermore, the degree of formation of new carbon–oxygen bond is higher than the degree of formation of new oxygen–hydrogen bond. As a result, the transition states become asymmetric, which reflects nucleophilic character of the addition of methanol associates **IIa–IIc** at the C=O bond of isocyanate **I**. While studying the addition of methanol associates at the C=N bond of isocyanate **I**, we also found advanced formation of the C–O bond as compared to N–H [1]. Comparison of the transition states in the two reaction pathways shows that the C=N bond dissociates to a greater extent than does the C=O bond in the addition at the carbonyl group. In both cases, the transition states are weakly polar: the calculated dipole

Table 3. Parameters f_{new} and f_{old} of transition states **TS1a–TS1c** in the reactions of phenyl isocyanate (**I**) with linear methanol associates **IIa–IIc**

Transition state	f_{new}(C–O)	f_{new}(O–H)	f_{old}(C–O)
TS1a	87.62	71.92	58.35
TS1b	84.04	69.48	44.87
TS1c	87.25	72.58	43.65

Table 4. Variation of the Gibbs energy ($\Delta G°$), enthalpy ($\Delta H°$), and entropy ($\Delta S°$) in the reactions of linear methanol associates **IIa–IIc** at the C=O bond of phenyl isocyanate (**I**) in the gas phase at 298 K

Reaction	$\Delta G°$, kJ/mol	$\Delta H°$, kJ/mol	$\Delta S°$, J mol^{-1} K^{-1}
I + IIa → IVa	59.5	9.3	–175.3
I + IIb → IVa + IIa	49.8	26.7	–77.7
I + IIc → IVa + IIb	47.0	35.5	–40.2

moments of transition states **TS1a–TS1c** are 3.3, 5.3, and 7.4 D, respectively.

Transition states **TS1b** and **TS1c** are then converted into unstable post-reaction complexes **IVb** and **IVc** whose decomposition yields methyl hydrogen phenylimidocarbonate (**IVa**) and methanol (**IIa**) or its dimer **IIb**. In the addition of methanol associates **IIa–IIc** at the C=N bond of **I**, the change in the Gibbs energy was negative, and the reactions were accompanied by evolution of heat. A different pattern is observed in the addition of **IIa–IIc** at the C=O bond (Table 4). These reactions are endothermic, and the change in the Gibbs energy is positive. Therefore, the reaction of methanol associates with isocyanate is reversible (the logarithms of the equilibrium constants range from –9 to –11 at 298 K). The enthalpy and entropy of the reaction conform to isokinetic relationship (7):

$$\Delta H\ (J/mol) = 42479 + 191\Delta S;\ R = 0.997. \qquad (7)$$

The relative variation in the Gibbs energies for the addition of methanol associates **IIa–IIc** at the C=O bond of isocyanate **I** is governed by the difference in the reaction entropies (Table 4). The same applies to the addition of **IIa–IIc** at the C=N bond of **I** [1].

The isomerization of imidocarbonate **IVa** into carbamate **V** is a unimolecular process involving concerted transition state **TS2** (Fig. 1). The isomerization is characterized by a considerable energy barrier (Table 1), and its height is determined mainly by the enthalpy factor. On the whole, the process is accompanied by an appreciable gain in energy.

Our results indicate that the most probable mechanism of the noncatalytic reactions of isocyanates with alcohols involves the C=N bond as reaction center, for the energy barriers along this reaction path are lower than those along the path with participation of the C=O group. We found no data consistent with ionic mechanism of the reaction of alcohols with isocyanates although that mechanism is often assumed while interpreting such reactions.

The two paths of the addition of alcohols at the isocyanato group, i.e., nucleophilic attacks at the C=N and C=O bonds, display many common features. Both paths involve formation of pre- and post-reaction complexes, and the transition states are cyclic, asymmetric, and late. Our results confirm the existing views according to which the nucleophilic reactivity of alcohols increases in parallel with the degree of their association. Our calculations showed that increase in the

degree of association of alcohols is accompanied by increase of their electron-donor power. Reactions at the C=N bond of isocyanates are more sensitive to variation of the donor properties of alcohol associates, as compared to the transformations involving the C=O bond, which may be interpreted in terms of frontier orbital interactions.

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