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I.P. Beletskaya on Her Jubilee

Acyl Iodides in Organic Synthesis:
III. Quantum-Chemical Study of the Reaction of Acyl Iodides and Acyl Chlorides with Methanol

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Abstract—The potential energy surface for reactions of acyl iodides and acyl chlorides with methanol was studied by quantum-chemical methods. Stereoelectronic parameters of the prereaction bimolecular complexes and possible reaction products were examined. Transition states were localized for the transformation of prereaction complexes into final products. Dual reactivity of acyl iodides toward methanol was explained in terms of similar activation parameters found for the four-center and S_N2 reaction mechanisms.

The results of our recent studies [1, 2] suggest that acyl iodides RC(O)I are promising deoxygenating, iodinating, and acylating reagents for organic synthesis. In particular, their reactions with aliphatic alcohols [1] and acyclic and cyclic ethers [2] were examined. The results of studying reactions of acyl iodides with carboxylic acids, esters, anhydrides, and acyl chlorides are submitted to publication. The reaction of acyl iodides with aliphatic alcohols could lead to formation of either the corresponding iodides or esters or mixtures of both these. The reaction direction depends on the acidity constant (pK_a) of the alcohol. Increase in pK_a favors formation of alkyl iodides. In the absence of catalyst, acyl chlorides RC(O)Cl (which may be regarded as analogs of acyl iodides) react with alcohols to give esters as the only product. The reaction of acyl halides with alcohols can be illustrated by the following general scheme:

$$RCOX \xrightarrow{R'OH} \begin{matrix} RCOOH + R'X \\ RCOOR' + HX \end{matrix}$$

$$X = Cl, I.$$
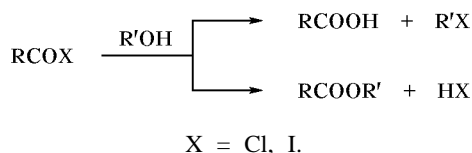
An obvious difference between the mechanisms of reactions of acyl iodides and acyl chlorides with alcohols and dual reactivity of acyl iodies prompted us to perform a quantum-chemical study of the reac-tions of acetyl iodide (**I**, R = Me) and acetyl chloride (**II**, R = Me) with the simplest aliphatic alcohol, methanol (**III**). We studied stereoelectronic parameters of prereaction bimolecular complexes **I** + **III** (**IV**) and **II** + **III** (**V**) and possible products of the reactions MeX + MeC(O)OH [X = I (**VIa**), Cl (**VIIa**)] and XH + MeC(O)OMe [X = I (**VIb**), Cl (**VIIb**)]. Transi-tion states for the transformation of prereaction com-plexes into final products were localized. The kinetic and thermodynamic parameters of these reactions were analyzed with regard to the halogen nature and transition state structure.

Topological properties of the systems under study in the configurational region of the reaction were calculated in terms of the B3LYP hybrid density functional method with the LANL2DZ basis set (ExtraBasis version) [3–7]. Complete geometry optimization of the molecular systems corresponding to transition structures ($\lambda = 1$, where λ is the number of negative Hessian eigenvalues for a given stationary point [8]) and energy minima ($\lambda = 0$) on the potential energy surface (PES) was performed up to a value of 10^{-5} a.u./bohr. While analyzing flat parts of the PES (for conformationally labile states which include prereaction complexes), the limiting values were set at a level of 10^{-6} a.u./bohr. Structures corresponding to energy minima on the PES were identified by moving along the gradient line from the saddle point

Table 1. Calculated[a] total energies E_{tot},[b] dipole moments μ, zero-point harmonic vibration energies (ZPE), least harmonic frequencies ω_i, bond lengths l, and angle φ

Structure	E_{tot}, a.u.	μ, D	ZPE, a.u.	ω_i, cm^{-1}	l(Me−X), Å	l(C−O), Å	φ(XCO), deg
I	−164.60227	3.24	0.04642	138 (264)	2.252 (2.21)	1.217 (1.18)	120.2 (125.0)
II	−168.16666	3.48 (2.71)	0.04729	151 (260)	1.909 (1.789)	1.212 (1.192)	119.5 (120.0)
III	−115.70843	2.20 (1.70)	0.05092	331	O−H, 0.979	1.459 (1.42)	COH, 110.8

[a] B3LYP/LANL2DZ ExtraBasis; experimental data [9, 10] are given in parentheses.
[b] 1 a.u. = 2622.9897 kJ/mol.

Table 2. Total energies E_{tot}, relative energies ΔE, numbers of negative Hessian eigenvalues λ, zero-point harmonic vibration energies (ZPE), imaginary or least harmonic frequencies $i\omega/\omega_1$, dipole moments μ, and Mulliken charges Z on the halogen atom for structures **IV–IX**, calculated by the B3LYP/LANL2DZ ExtraBasis method

Structure	E_{tot}, a.u.	ΔE, kJ/mol	λ	ZPE, a.u.	$i\omega/\omega_1$, cm^{-1}	μ, D	Z
IVa	−280.31618	7.9	0	0.09858	16	4.64	0.002
IVb	−280.31920	0	0	0.09886	27	3.62	−0.060
Va	−283.88564	0	0	0.10006	24	2.35	−0.106
Vb	−283.88486	2.1	0	0.09983	25	3.13	−0.171
VIa	−280.35303	−88.7	0	0.09980	34	1.22	0.019
VIb	−280.32180	−6.8	0	0.09608	25	8.60	−0.160
VIIa	−283.91301	−71.8	0	0.10095	40	1.42	−0.134
VIIb	−283.89083	−13.6	0	0.09776	36	9.30	−0.320
VIIIa	−280.28917	78.8	1	0.09889	i179	8.94	−0.680
VIIIb	−280.28892	79.4	1	0.09854	i198	8.62	−0.436
IXa	−283.81791	177.6	1	0.09963	i247	7.50	−0.529
IXb	−283.85491	80.6	1	0.09927	i238	7.54	−0.500

to the nearest critical points. For this purpose, an initial small shift along the transition vector was set, which allowed correct determination of the gradient reaction path.

Table 1 contains the calculated energy parameters and principal geometric parameters of isolated molecules **I–III**, as well as their electric dipole moments and vibrational frequencies; for comparison, some experimental data are also given. The calculation results for the reaction of methanol with acetyl halides predict the existence on the PES of two most stable states of bimolecular complexes **IV** and **V** which are stabilized by intermolecular hydrogen bonds O−H···O and O−H···X (Fig. 1). The energy difference between these states is insignificant (Table 2). In the reaction with acetyl iodide, the most stable is prereaction complex **IVb** having O−H···I hydrogen bond. By contrast, structure **Va** stabilized by O−H···O bonding is more stable for acetyl chloride (Table 2). The energy of stabilization of prereaction bimolecular complexes **IVa**, **IVb** and **Va**, **Vb** relative to the

isolated fragments (with no ZPE taken into account) is, respectively, 14.4, 22.3, 27.5, and 25.6 kJ/mol (Tables 1, 2). With a correction for ZPE, these values are reduced to 11.1, 18.3, 22.8, and 21.4 kJ/mol, respectively. Products of the above exchange reactions, both those leading to formation of methyl acetate (**VIb**, **VIIb**; Fig. 2) and methyl iodide (**VIa**) or methyl chloride (**VIIa**), are thermodynamically more stable than the corresponding initial bimolecular complexes **IVa**, **IVb** and **Va**, **Vb** (Table 2). The formation of complex **VIa** is more favorable than the formation of **VIb** by 81.9 kJ/mol. An analogous pattern (from the viewpoint of thermodynamics) is observed in the reaction of **II** with **III**. The calculated heat of formation of methyl chloride is greater by 58.2 kJ/mol than the heat of formation of HCl, which contradicts the experimental data. Presumably, the main factor determining the direction of the reactions under study is kinetic control. With the goal of estimating their activation parameters we localized transition states for the transformation of the initial
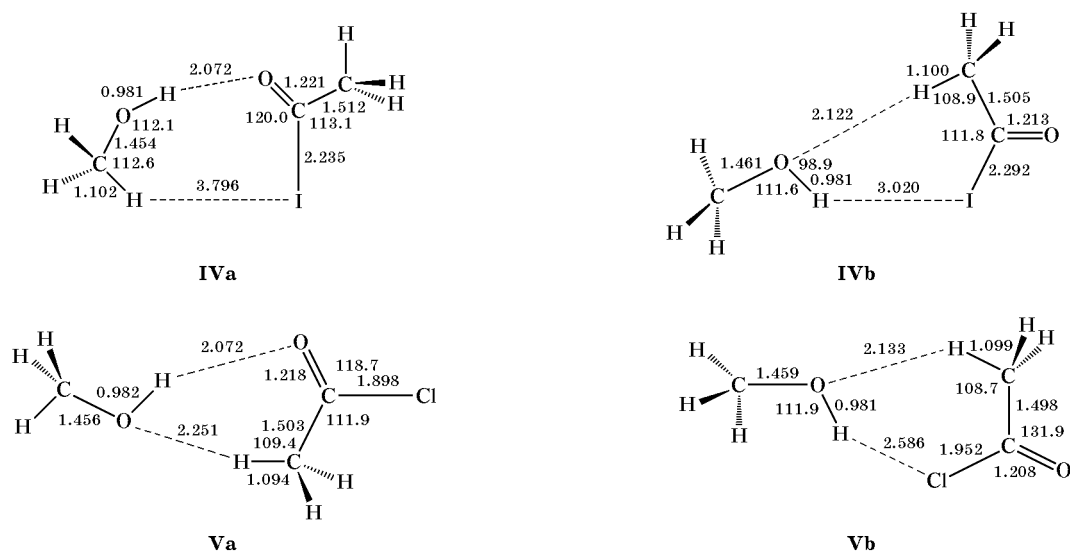
Fig. 1. Geometric parameters (bond lengths, Å, and bond angles, deg) of prereaction bimolecular complexes **IVa**, **IVb**, **Va**, and **Vb**.
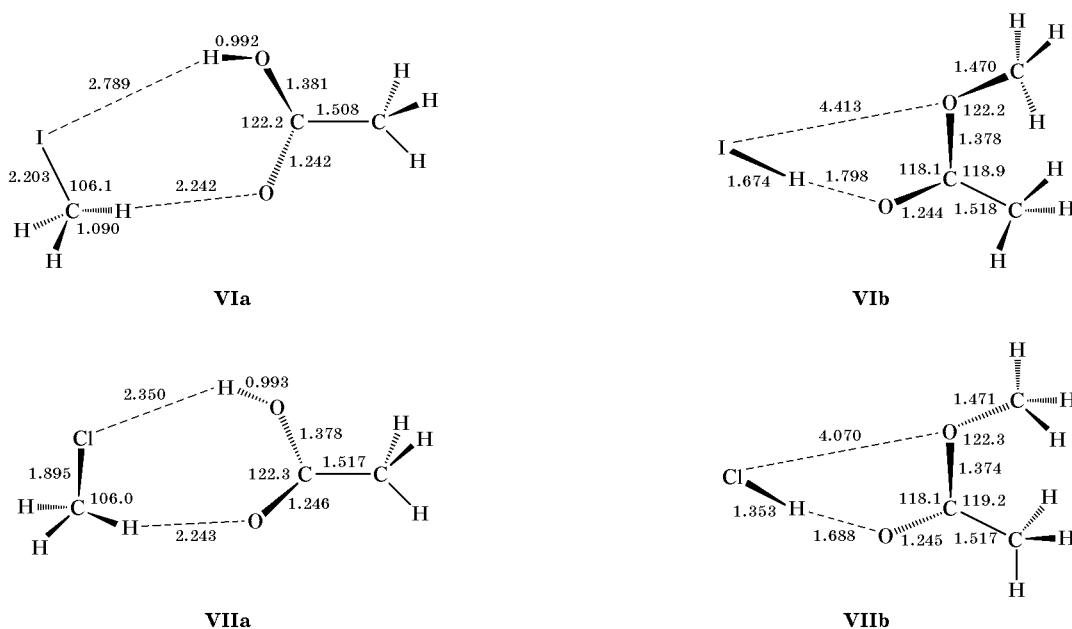

Fig. 2. Geometric parameters (bond lengths, Å, and bond angles, deg) of molecular systems **VIa**, **VIb**, **VIIa**, and **VIIb**.

bimolecular complexes into final products (**IVa** →
VIa, **IVb** → **VIb**, **Va** → **VIIa**, and **Vb** → **VIIb**;
transition state structures **VIIIa**, **VIIIb**, **IXa**, and **IXb**,
respectively; Fig. 3).

The transitions **IVa** → **VIa** and **IVb** → **VIb** in
the reaction with acetyl iodide are characterized by
similar activation energies (Table 2). Therefore, the
probabilities for the reaction to take both the above
pathways are equal. This is consistent with the experi-

mental data. We previously showed that the reactions
of acetyl iodide (**I**) with methanol and ethanol give
rise to equimolar mixtures of the corresponding alkyl
iodides and esters [1]. The simulated transition state
for the transformation **IVb** → **VIb** has a four-center
structure with a high degree of charge separation. It
is characterized by a considerable electron density
transfer to the halogen atom (Table 2). Even greater
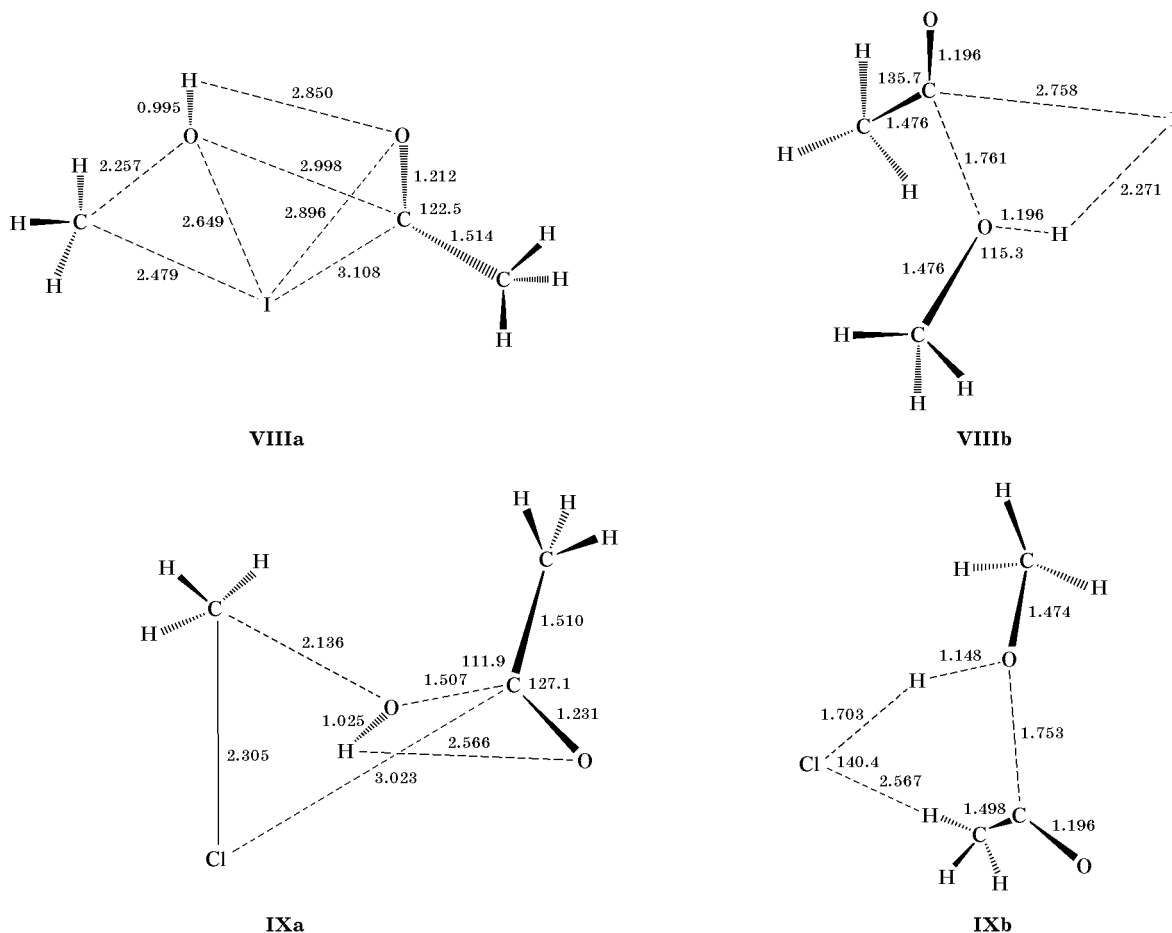charge separation and electron density transfer to the

Fig. 3. Geometric parameters (bond lengths, Å, and bond angles, deg) of transition states **VIIIa**, **VIIIb**, **IXa**, and **IXb**.

iodine atom (Table 2) were found for the transition state **IVa** → **VIa** (Fig. 3).

Analogous reactions with participation of chlorine lead to different results. The energy of transition state in the formation of HCl differs only slightly from the energy of activation of a similar reaction involving acetyl iodide. The activated complex is a four-center state with a lesser degree of charge separation (Fig. 3, Table 2). In the formation of methyl chloride, the activation energy is considerably higher than in the case of methyl iodide (Table 2). However, the favorable value of ΔH for the formation of methyl chloride suggests that this process is possible in the presence of catalysts capable of reducing the activation barrier (Lewis acids). Examples of such reactions are well known [11, 12].

Our results can be interpreted in terms of the dynamics of variation of the polyfunctional reaction coordinate. In the formation of HX, complete rupture of the C–X bond follows proton migration to the halogen atom, whereas in the formation of methyl halide, the principal constituent of the reaction coordinate is dissociation of the C–X bond. Taking into account considerable difference in the strengths of the C–Cl and C–I bonds (76.7 and 46.0 kcal/mol, respectively [10]), the large difference in the activation parameters of these reactions becomes clearly understood. Also, displacement of equilibrium toward formation of alkyl iodides with rise in pK_a of alcohols may be explained. Increase in pK_a means that the O–H bond becomes stronger; therefore, the activation barrier for the four-center reaction mechanism increases, and the S_N2 mechanism involving iodide ion as nucleophile predominates. In the reactions with acyl chlorides, no mechanism altering occurs because of the large difference in the activation barriers for the four-center and S_N2 mechanisms.

The dipole moments of molecular systems in the critical points of the PES suggest that, in going from the gas phase to polar solvents, the activation barrier should become lower, products of the reaction **IVb** (**Vb**) → **VIb** (**VIIb**) should be stabilized, and

those of the reaction **IVa** (**Va**) → **VIa** (**VIIa**) should be destabilized relative to the prereaction bimolecular complexes.

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