Synthesis on the basis of electrogenerated carbenes 9.* Quantum chemical investigation of $S_N2$ reactions of polyhalomethanes and their anions

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A series of $S_N2$ reactions with halomethanes as substrates and the corresponding anions as nucleophiles were studied by the semiempirical MNDO and AM1 methods, taking into account solvent effects. Analysis of the kinetics, structures of reagents, intermediates and products, and charge distribution in them allows one to draw the conclusion that the retardation of $S_N2$ reactions is stronger in solvents than in the gas phase, and the rates of reactions involving anions with a lower number of halogen atoms are higher.

Key words: semiempirical calculation, MNDO, AM1; $S_N2$ reactions, transition states, structure; chloro- and bromomethane anions, halomethanes; accounting for solvation, point dipole method.

Reactions of nucleophilic substitution ($S_N2$ reactions) in the aliphatic series can be attributed to processes that are being studied mostly theoretically (see Refs. 2–8). Results of various studies, including quantum chemical investigations, form a basis for many modern theories concerning mechanisms of organic reactions in solution and solvent effects on their character. For example, several programs that make it possible to take into account solvation effects determining rates of $S_N2$ reactions in the medium have appeared recently. They use various approaches for reproducing solvation effects: nonempirical (e.g., Monte Carlo), semiempirical (the Born–Kirkwood–Onsager model), and combined approaches (for example, the method of Monte Carlo statistical mechanics with combined potential (quantum chemical and molecular mechanical), AM1/TIP3P). One such approach based on the point dipole methods is used in this work for quantum chemical study of $S_N2$ reactions involving polyhalomethanes and anions generated from them.

We considered the following reactions of nucleophilic substitution:

$\text{CCl}_3^- + \text{CCl}_4 \rightarrow \text{Cl}_2\text{C}--\text{CCl}_3 + \text{Cl}^-$,

$\text{CCl}_3^- + \text{HCCl}_3 \rightarrow \text{HCl}_2\text{C}--\text{CCl}_3 + \text{Cl}^-$.  

$\text{CBr}_3^- + \text{CBr}_4 \rightarrow \text{Br}_2\text{C}--\text{CBr}_3 + \text{Br}^-$,

$\text{CBr}_3^- + \text{HCBr}_3 \rightarrow \text{Br}_2\text{C}--\text{CBr}_3 + \text{Br}^-$.  

These processes can be alternative reactions to $\alpha$-elimination, forming halomethane anions under the conditions of both phase transfer catalysis and their electrochemical generation discussed in our previous publications. Therefore, in our opinion, the analysis of thermodynamic and structural parameters of reactions...
(1)–(14), depending on electronic structures of halo-
methanes and anions and polar properties of the medium, is of general interest.

**Calculation procedure**

The calculations were performed by the MNDO\textsuperscript{12} and AM1\textsuperscript{13} semiempirical methods, which are somewhat less rigorous than \textit{ab initio} methods, but allow one to consider a wide range of \textit{S}_{N}2 reactions. In addition, a semiempirical method, in particular, MNDO, in terms of the point dipole model\textsuperscript{14} makes it possible to qualitatively take into account solvation effects for the reactions considered with a low expenditure of computer time. Transition states were determined by the MNDO and AM1 methods, using the SADDLE procedure from the MOPAC program package followed by refinement of their geometry by minimization of the gradient norm. The calculation was performed by the previously described procedure.\textsuperscript{15}

Cross sections of potential energy surfaces (PES) were developed in terms of MNDO by the reaction coordinate method. It should be mentioned, however, that nucleophilic substitution is one of the processes for which the choice of the reaction coordinate is not evident. If the length of the forming or breaking bond is chosen as such a coordinate (as recommended, \textit{e.g.}, in Ref. 16), at small distances a slight change in any of them causes a strong change in another bond length.\textsuperscript{17} Therefore, one can hardly expect to obtain the true PES cross section in this case, in particular, to correctly determine ion-dipole complexes on the PES. Therefore, the difference between the distances was chosen as a reaction coordinate

\[
AR = Rx...c - Rc...y.
\]

In fact, this calculation method means the search of a minimum on PES along the axes

\[
Rx...c = \Delta R + Rc...y
\]

and allows one to find one point on the trajectory of the movement of reagents in the reaction course at the fixed value of \(\Delta R\). The energies of the transition states determined by this method coincide well with those obtained by the SADDLE procedure, which confirms the correctness of the choice of the reaction coordinate. The method suggested allows one to calculate the energy of the system in any point of the PES cross section along the reaction coordinate. In particular, energies of possible minima and, hence, true reaction barriers with complicated potential profiles with intrinsic activation barriers can be efficiently determined. Nucleophilic substitution belongs to such reactions.

**Choice of solvents.** In this work, the following solvents were chosen as models for estimation of the energy of the considered reactions in liquid media: high polar \(\text{H}_{2}\text{O}\), medium polar dimethyl sulfoxide (DMSO), and low polar methylene chloride (\(\text{CH}_{2}\text{Cl}_{2}\)). This choice makes it possible to follow the change in thermal effects and activation energies of reactions as the polarity of a medium decreases. The corresponding parameters of the solvents are taken from Ref. 18.

**Results and Discussion**

**Thermodynamics of reactions.** The heats of reactions (1)–(14) were calculated by the MNDO and AM1 methods with complete optimization of their geometries. The results of the calculations and the experimental data are presented in Table 1. It can easily be seen that the values obtained by the MNDO method are closer to the experimental data except for reaction (1), whose strong divergence from the experiment is caused by the fact that the MNDO method overestimates the stability of the \(\text{CCl}_{3}^{-}\) carbanion. The AM1 method gives systematically decreased values of \(\Delta H\) of the reactions (see Table 1) mainly due to its considerable underestimation of the stability of halogen anions.\textsuperscript{19} Therefore, the positive values of \(\Delta H\) of reactions (8) and (9) obtained by the AM1 calculation are obviously inflated and will not be taken into consideration.

The data in Table 1 allows one to draw a conclusion that the considered \(\text{S}_{N}2\) reactions are thermodynamically favorable in the gas phase. Although the absolute values of \(\Delta H\) obtained by the MNDO and AM1 methods sometimes strongly differ, both methods equally well reflect their relative changes. The following tendency is revealed: in the series considered the heats of reactions of nucleophilic substitution mainly depend on the number of Hal atoms in a carbanion and increase as their

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* The experimental values of the heats of formation of anions and neutral molecules for calculating reaction heats are taken from Ref. 20.