An Oxygen Exchange of Arsenate and Alkylarsonate Ions with Water

Nobuko NIWA, Midori FUSHIMI, Masayasu IIDA, Yuko HORIE, Shinichi YAMABE,† and Akiko OKUMURA*
Department of Chemistry, Faculty of Science, Nara Women's University, Kita-uoya-nishi-machi, Nara 630
†Department of Chemistry, Nara University of Education, Takabatake-cho, Nara 630
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The oxygen exchange rates, R's, between the alkylarsonates (methyl- and butyl-) and water were measured over the pH range greater than 9 and at 30 °C. The rates were analyzed in terms of the rate law, $R=k_1[R'\text{-}AsO_3H^-]+k_2[R'\text{-}AsO_3^{2-}]$ (R'-; alkyl-) to obtain k_1 to be 6.64×10^{-4} s^{-1} for methyl- and 4.38×10^{-4} s^{-1} for butylarsonate ions, respectively. The first-order oxygen exchange rate constants, k_1's, on the alkylarsonate univalent anions (methyl and butyl) are almost the same values, which indicates that the steric effect on the rate is absent. The rate constants, k_1's, correlate well with energy levels of the lowest unoccupied molecular orbitals (E_{LUMO}'s) of univalent anions of arsenic, arsenious, and alkylarsonic acids.

The important role of phosphoric acid and its derivatives in biochemical processes is known-well. There are many studies of the hydrolysis of organic phosphates[1] and the oxygen exchange of phosphoric acid with water.[2] The As and P atoms belong to the nonmetal Va group and consequently arsenic and phosphoric acids have similarity in structures and physical properties in solution. On the other hand, the difference of reactivity between them is enormous; the oxoanions of arsenic are reactive, while those of phosphorus are stable and unreactive. Many biochemical effects seem to be due to the ability of arsenic(V) to mimic the analogous phosphates; arsenate may substitute for phosphate as a substrate in certain phosphorylation[3] and some enzymatic arsenolyses.[4] The investigation of the behavior of arsenic(V) is important and is expected to shed light on the reaction mechanism of phosphoric(V) in biological systems.

While the oxygen exchange reactions between the oxoanions of phosphorus and water have been extensively studied, those of oxoanions of arsenic are rather few.[5–7]

The difficulty of the latter measurement by ^{18}O tracer method was mainly in the separation process of the oxoanions from the solution for isotopic oxygen analyses. As stated in a previous paper,[6] on the precipitation of the oxoanions by metal ions, the oxygen exchange of the oxoanions of arsenic is induced. In the case of some alkylarsonates, any precipitant could not separate oxoanions from the solution. NMR instrumentation recently available has alleviated these problems, but there still remains a difficulty in the preparation of ^{17}O-enriched compounds for ^{17}O NMR technique.

However, it is important to study kinetics of the oxygen exchange on As, because it provides information of the microscopic interaction between oxoanion and solvent water and between oxoanions in the solution.[6–10] Furthermore, the detailed kinetic data of the oxygen exchange of arsenate ions may explore the possibility of the use of ^{18}O-labelled arsenate in biochemical tracer work.

Here, we present new rate constants of R'-As(OH)O_2^- ions, where R' is the alkyl group (R'=methyl or butyl). It is of mechanistic interest to know how the alkyl substituent affects the oxygen-exchange rate. The long chain of the butyl would block the nucleophilic attack of a water molecule. After the first-order rate constants are measured, those substituent effects are investigated with the aid of the ab initio molecular orbital (MO) calculation. The relation between the electronic property and the reactivity of arsenate and alkylarsonate ions is sought. In particular, it should be carefully checked what kind of the isomer of the substrate is involved in the oxygen exchange reaction. As atom may have 3, 5, or 7 chemical bonds, and this freedom might be related to the intervention of unexpected isomers and subsequently to the anomalous rate constants. This is a pioneer work which deals with the S_N2 reaction of the As atom systematically.

Experimental and Computational

Materials. Methyl- and butylarsonates were prepared according to Quick.[11] Methylarsonate was recrystallized several times from aqueous ethanol solution (50 vol%). The methylarsonic acid derived from the purified salt has a melting point of 161 °C (161 °C[11]). The C and H contents by elemental analyses are: Found: C, 8.66; H, 3.62%. Calcd for $CH_3AsO_3H_2$: C, 8.58; H, 3.60%. A crude product of butylarsonate was acidified to form arsonic acid, which was purified by the crystallization from water and ethanol. The melting point of the acid are 161 °C (159—160 °C[11]), and elemental analyses gave: Found: C, 26.53; H, 6.12%. Calcd for $C_4H_9AsO_3H_2$: C, 26.40; H, 6.10%.

Rate Measurements. The oxygen-exchange rate of methylarsonate was followed by measuring the decrease in the ^{18}O contents of arsonate upon diluting an isotopically equilibrated solution of $CH_3AsO_3Na_2$ in [^{18}O]water with a large amount of isotopically normal water. A portion of the solution was drawn periodically and the arsonate was recovered by freeze-dry method, its oxygen being converted into carbon dioxide by the guanidinium chloride method.[12] The isotopic analysis of carbon dioxide was made on a Hitachi RMS-I-type mass spectrometer.

The rates of oxygen exchange of butylarsonate were obtained by ^{17}O NMR method. A weighed amount of butylarsonate enriched in ^{17}O was dissolved into 3 ml of water in an ice bath. After pH adjustment, the solution was transferred to a sample tube for running the NMR spectra. In the measurements, both the decrease in the intensity of ^{17}O-signal of the arsonate and the increase in that of water were followed. The rates on both the signals are satisfactorily agreed. ^{17}O NMR spectra were recorded at 36.6 MHz on a FT-NMR spectrometer, JEOL-GX270. The ^{17}O-chemical shift for n-$C_4H_9AsO_3Na_2$ is downfield from water by 130 ppm.

The rate of oxygen exchange, R, was calculated by means of the formulas:

$$R = -\frac{1}{t}\frac{[\text{arsonate}][H_2O]}{3[\text{arsonate}]+[H_2O]}\ln\frac{*O_t - *O_\infty}{*O_0 - *O_\infty}$$

where $*O_0$, $*O_t$, and $*O_\infty$ are ^{18}O (for methylarsonate) or ^{17}O (for butylarsonate) contents at the times 0, t, and infinity, respectively. [arsonate] and [H_2O] are the molar concentrations (mol dm^{-3}) of the arsonates and water, respectively.

The Dissociation Constants of Arsonic Acids. These were determined by the potentiometric titration at 30 °C and I=0.55 mol dm^{-3}. The values of pK_2 are 8.50 for methylarsonic acid and 8.88 for butylarsonic acid.

Ab Initio Molecular-Orbital (MO) Calculation. To compare the reactivity of arsonates for the oxygen exchange with each other, we performed an MO calculation on five substrates with the STO-3G* basis set (STO-3G plus six d orbitals on arsenic). All the electrons are explicitly considered, and the geometries are fully optimized using the GAUSSIAN 82 program.[13]

Results of Kinetics

The exchange rates for the two reactions were measured at 30 °C and over the pH range between 9 and 12 where the dominating ionic species of arsonates are R′-AsO_3^{2-} and R′-AsO_3H^- (R′=CH_3 or n-C_4H_9). The results are shown in Table 1.

The dependence of the rate on the concentration of arsonates was studied at pH 10.6 for methylarsonate (**A**) and pH 10.9 for butylarsonate (**B**). The plots of $\log_{10} R$ against $\log_{10}$[arsonate] give the straight lines with slopes of 0.92 for **A** and 1.07 for **B**, respectively (Fig. 1). The first-order dependence observed in Fig. 1 suggests that the oxygen exchange of arsonates proceeds through two parallel paths:

$$\text{R′-AsO}_3\text{H}^- + \text{H}_2{*}\text{O} \overset{k_1}{\rightleftharpoons} \text{R′-AsO}_2{*}\text{OH}^- + \text{H}_2\text{O}$$

$$\text{R′-AsO}_3^{2-} + \text{H}_2{*}\text{O} \overset{k_2}{\rightleftharpoons} \text{R′-AsO}_2{*}\text{O}^{2-} + \text{H}_2\text{O}$$

and the exchange rate law may be written as:

$$R = k_1[\text{R′-AsO}_3\text{H}^-] + k_2[\text{R′-AsO}_3^{2-}]$$

By the use of this relation, the exchange rates shown in Table 1 were analyzed and the values of k_1 and k_2 are obtained to be 6.64×10^{-4} s^{-1} and 2.69×10^{-4} s^{-1} for methylarsonate and 4.38×10^{-4} s^{-1} and 9.33×10^{-5} s^{-1} for butylarsonate, respectively. Noteworthy is the result that the four rate constants are of the same order, and a noticeable steric or hydrophobic effect of the butyl substituent is not observed.

Table 1. The pH Dependence of the Oxygen Exchange Rates of Methyl- and Butylarsonates (30 °C and I=0.55 mol dm^{-3}. [methylarsonate]=0.1 mol dm^{-3}, [butylarsonate]=0.2 mol dm^{-3})

R′-	pH	$R/10^{-5}$ mol dm^{-3} s^{-1}
CH_3-	9.17	5.07
	9.57	3.41
	10.02	2.91
	10.10	3.03
	10.13	2.36
	10.52	2.50
	10.60	2.89
n-C_4H_9-	9.01	4.68
	9.50	3.33
	9.71	2.71
	10.56	2.11
	11.11	1.69
	12.31	1.90

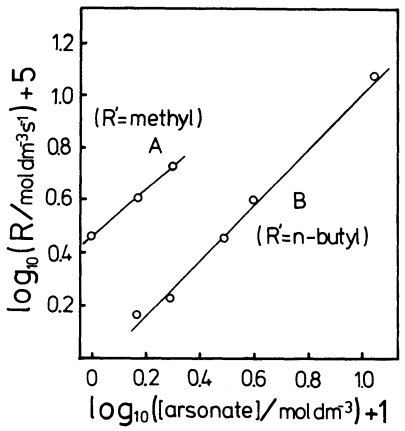


Fig. 1. The dependence of the exchange rate, R, on the concentration of arsonates.

The rate constants of the oxygen exchange between univalent anoin of arsonate and water, k_1's, thus obtained were used in the following discussion.

Computational Results and Discussion

First, measured exchange-rate constants [$k_1^{(A)}$, $k_1^{(B)}$, $k_1^{(C)}$, $k_1^{(D)}$] are compared with each other. $k_1^{(A)}$ and $k_1^{(B)}$ are presented in the previous section, and $k_1^{(C)}$ [6] and $k_1^{(D)}$ [7] are taken from literatures.

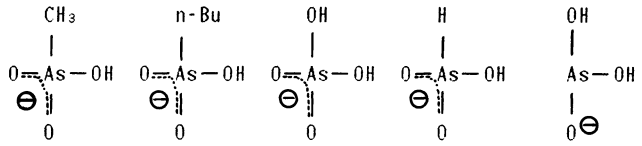
$$CH_3AsO_3H^- + H_2{*}O \longrightarrow CH_3AsO_2{*}OH^- + H_2O \quad \text{(A)}$$
$$k_1^{(A)} = 6.6\times10^{-4}\ \text{s}^{-1}$$

$$n\text{-}C_4H_9AsO_3H^- + H_2{*}O \longrightarrow n\text{-}C_4H_9AsO_2{*}OH^- + H_2O \quad \text{(B)}$$
$$k_1^{(B)} = 4.4\times10^{-4}\ \text{s}^{-1}$$

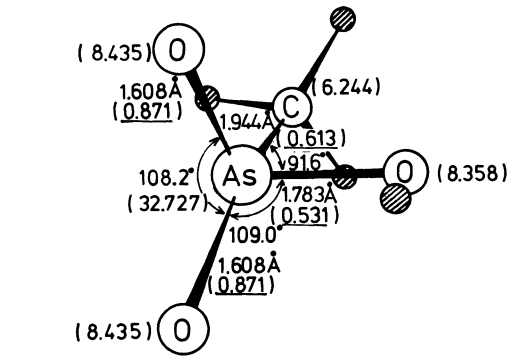
$$H_2AsO_4^- + H_2{}^*O \longrightarrow H_2AsO_3{}^*O^- + H_2O \quad (C)$$
$$k_1^{(C)} = 1.0\times10^{-4}\ s^{-1}$$

$$H_2AsO_3^- + H_2{}^*O \longrightarrow H_2AsO_2{}^*O^- + H_2O \quad (D)$$
$$k_1^{(D)} = 167\ s^{-1}$$

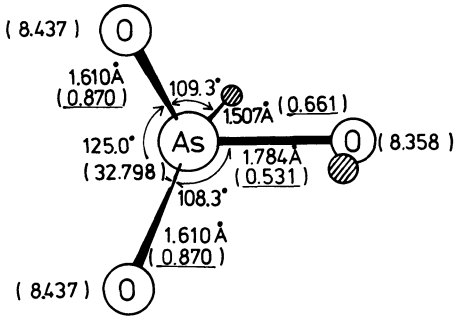
The relation of $k_1^{(D)} \gg k_1^{(A)} \simeq k_1^{(B)} > k_1^{(C)}$ is recognized. It seems to be curious that the $k_1^{(D)}$ (R′=H) is much larger than $k_1^{(A)}$ (R′=methyl) and $k_1^{(B)}$ (R′=butyl). Some anomalies for the large reactivity of H-AsO_3H^- must be present. To analyze this trend, an MO calculation is made for the following substrates.



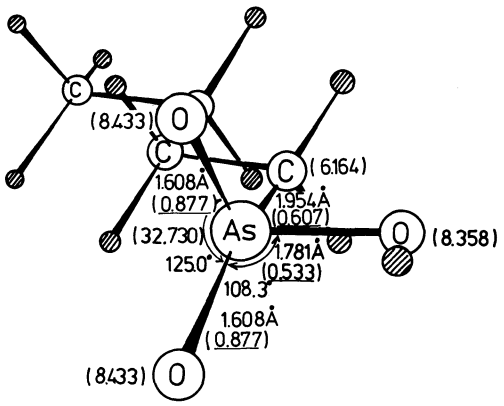
For $H_2AsO_3^-$, **D**, **Db** is an isomer of **Da**. The anomalous value of $k_1^{(D)}$ may be related to the isomer. Optimized geometries of **A**, **B**, **C**, **Da**, and **Db** are



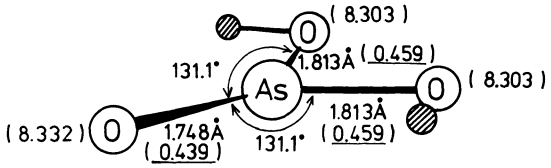
A



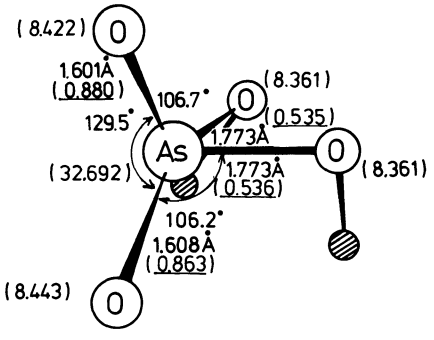
Da



B



Db

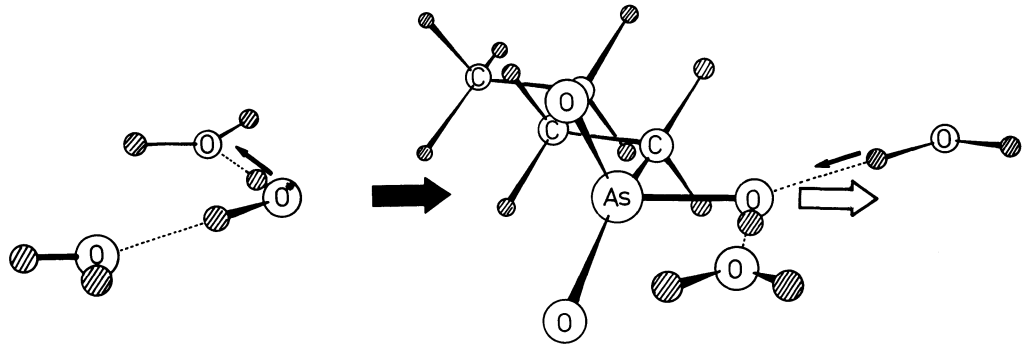


C

Fig. 2. Geometries of arsenate and alkylarsonate ions optimized with the STO-3G* basis set. Shaded circles denote hydrogen atoms. Values in parentheses stand for the atomic electronic density, and underlined ones do the atom-atom bonding populations.

exhibited in Fig. 2. The As–O bond length 1.78 Å of **A** and **B** is comparable to 1.71 Å of the crystal data of propylarsonic acid.[14] Likewise, the As–O 1.61 Å and As–C 1.94 (and 1.95) Å are comparable to 1.65 Å and 1.92 Å, respectively.[14]

First, the presence or the absence of the steric or hydrophobic effect by the butyl group is examind in Fig. 3. The figure shows the lowest unoccupied molecular orbital (LUMO) which undergoes the charge transfer from the nucleophile, water. The orbital extention of LUMO clearly demonstrates that H_2O attacks the back side of the As–OH bond. The butyl chain is distant from the channel of the nucleophilic attack, and the result that the path is not blocked by the alkyl chain is related to $k_1^{(A)} \simeq k_1^{(B)}$ (no steric effect).



Second, the anomalously large value of $k_1^{(D)}$ is interpreted in terms of the computed data, i.e. the energy level of LUMO (E_{LUMO}). E_{LUMO}'s of **A**, **B**, **C**, **Da**, and **Db** vs. rate constants are plotted in Fig. 4. It is found that not E_{LUMO}(**Da**) but E_{LUMO}(**Db**) is in the line. Thus, $H_2AsO_3^-$ is present in the form of $(HO)_2AsO^-$, **Db**, which is consistent with the data of Raman spectra in aqueous solution.[15]

This finding of arsenious acid is the first case in which the structure of the oxoanion in the solution is identified on the basis of the kinetic results of the oxygen exchange. The combined treatment of the kinetic results and MO calculation used in this work seems to be applicable to S_N2 reaction on the heavy atoms other than As.

Concluding Remarks

In this study, rate constants of oxygen exchange of alkylarsonate ions were measured. It is found that the steric effect does not dominate the rates. In the theoretical side, it is confirmed that the alkyl group is apart from the S_N2 path and therefore the rate is insensitive to the size of the alkyl chain. The remarkably large rate constant of the $H_2AsO_3^-$ is ascribed to the low-lying E_{LUMO} of [not $H\text{-}As(OH)O_2^-$] but $(OH)_2AsO^-$.

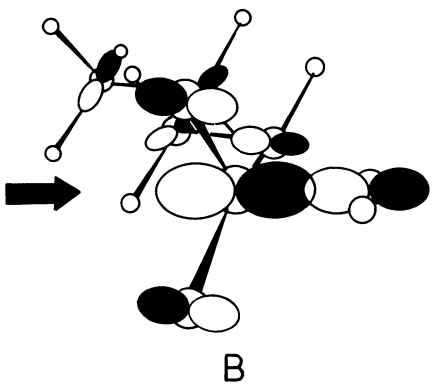


Fig. 3. The sketch of the orbital extension of the frontier orbital, LUMO, of the butylarsonate ion. The bold arrow indicates the direction of the nucleophilic attack of a water molecule.

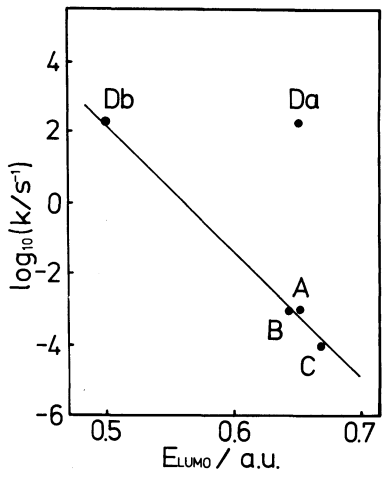


Fig. 4. The correlation between the energy of the lowest unoccupied molecular orbital (E_{LUMO}) and the logarithm of the rate constant at 30 °C for substrates **A**, **B**, **C**, and **D**. 1 a.u.=1 hartree=2.626×10^6 J mol^{-1}.

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