Neighboring Group Participation by Carbonyl Oxygen in Nucleophilic Substitution. Hydrolyses of [(9-Oxobenzonorbornen-2-yl)methyl]methyl(*p*-nitrophenyl)sulfonium Tetrafluoroborate

Tadashi Irie and Hiroshi Tanida*

Shionogi Research Laboratory, Shionogi & Co., Ltd., Fukushima-ku, Osaka, 553 Japan

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Evidence was obtained for participation of a hydration equilibrium of a carbonyl compound in an S_N2 reaction. Hydrolysis of [(9-oxobenzonorbornen-*exo*-2-yl)methyl]methyl(*p*-nitrophenyl)sulfonium tetrafluoroborate (**10**) in aqueous buffer medium afforded in quantitative yield an alcohol of retained structure, (9-oxobenzonorbornen-*exo*-2-yl)methanol (**9**), as a result of nucleophilic attack of water at the sterically more hindered methylene carbon α to the sulfonium sulfur. In contrast, the same reactions of the *endo*-2-yl epimer (**11**) and isobutylmethyl(*p*-nitrophenyl)sulfonium perchlorate (**15**, a model compound) occurred at the less hindered methyl carbon, entirely for **11** and predominantly for **15**. The overall rate law for the hydrolysis of **10** is suggested to be rate $= [S]\{k_{H_2O} + k_H[H^+] + k_{OH}[OH^-] + k_{HB}[HB] + k_B[B] + k_{BT,OH}[B]_T[OH^-]\}$. All the coefficients k determined were in almost the same order of magnitude as the corresponding k's recently reported for the hydrolysis of the *anti*-9-hydroxybenzonorbornene derivative (**4**),[7] which involves participation by hydroxyl oxygen. When k_{H_2O} and k_{OH} were compared with the corresponding rates of another model, dimethyl(*p*-nitrophenyl)sulfonium perchlorate (**14**), the relative reactivities were calculated as 240 and 10^6, respectively, and the effective molarity (EM) was calculated as 1.3×10^4 M.

Intramolecular reactions, in which the reactants are covalently bonded to one another, usually proceed much faster than the analogous intermolecular reaction. These intramolecular reactions are frequently taken as models for enzyme-catalyzed reactions where the reactants are held close together in the enzyme–substrate complex. A very important factor for rate enhancement of the intramolecular reactions is neighboring group participation. In an enzymic system, nucleophilic attack at a carbon atom adjacent to electron-deficient trivalent sulfur (sulfonium compounds) is exhibited by *S*-adenosylmethionine, which is a principal coenzyme associated with biological alkylation.[1-3] However, in the case of nonenzymic chemical reactions, sulfonium compounds are resistant to intermolecular attack by nucleophiles and particularly by oxygen nucleophiles.[4,5] A model reaction for biological alkylation involving neighboring hydroxyl participation was first reported in the hydrolysis of *cis*-cyclopentanol derivative **1** which undergoes intramolecular attack of the hydroxyl group on the carbon α to the trivalent sulfur, affording *cis*-2-oxabicyclo[3.3.0]octane (**2**) and *p*-nitro(methylthio)benzene (**3**) (eq 1).[6] Then we reported a similar ring closure with the 9-hydroxybenzonorbornene derivative **4**, which proceeded in aqueous buffer medium with general-base- and -acid-catalysis effects.[7] Working with carbonium ion reactions, we observed in the benzonorbornene system a new type of neighboring group participation by carbonyl oxygen. Solvolysis of brosylate **6** in aqueous acetone proceeded involving transformation of the keto group into the diol **7** with addition of water (hydration equilibrium of a carbonyl compound) followed by participation of one of the thus formed hydroxyl groups in the cationic reaction center (the transition state involves a five-membered ring), leading to an intramolecularly cyclized hemiketal intermediate **8**, which decomposed to give alcohol **9** by the formed *p*-bromobenzenesulfonic acid[8] (eq 3). Rate enhancement and sole formation of the substitution product **9** with retained structure were observed. In this paper, we report facile hydrolysis of a related sulfonium salt, [(9-oxobenzonorbornen-*exo*-2-yl)methyl]-

Chart I

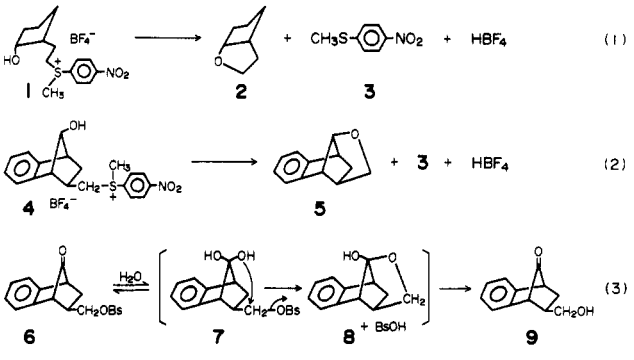
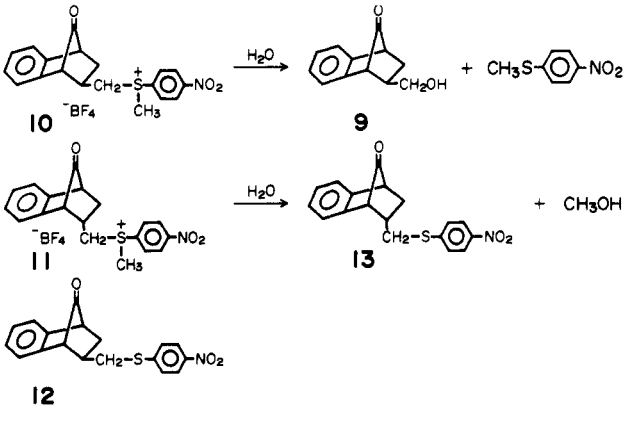


Chart II



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methyl(*p*-nitrophenyl)sulfonium tetrafluoroborate (**10**), which suggests participation by carbonyl oxygen in nucleophilic substitution with general-base- and -acid-catalysis effects.

Results

Methylation of the recently reported (9-oxobenzonorbornen-*exo*-2-yl)methyl *p*-nitrophenyl sulfide (**12**) and its endo epimer (**13**) was performed with silver tetrafluoroborate and methyl iodide in nitromethane to give **10** and **11**, respectively. Hydrolysis of **10** in buffered medium was carried out under relatively mild conditions with quantitative formation of the keto alcohol **9** of retained structure and *p*-nitro(methylthio)benzene; the former was also the sole product of the brosylate hydrolysis (eq 3). On the other hand, the hydrolysis of **11** was very slow and resulted in demethylation giving **13**.

Kinetics. The reactions of **10** were performed in water medium in the pH range of 1.50–10.10. The buffer systems employed were HCl,NaOH–citric acid, CH_3COONa–CH_3COOH, Na_2HPO_4–KH_2PO_4, and Na_2CO_3–$NaHCO_3$. The rates were followed by the increasing intensities of the UV maximum (350 nm) due to *p*-nitro(methylthio)benzene formation. The effects of varying the buffer ion concentration at a constant ionic strength (μ = 1.0 M) at several pH values were determined and are summarized in Table I. The rate constants k_1, extrapolated to 25.0 °C, are used for discussion.

Calculations. As described in our previous publication,[7] the rate constant k_1 in a buffer medium may be defined on the basis of general-acid–base catalysis.

$$k_1 = k_B[B] + k_{HB}[HB] + k_{OH}[OH^-] + k_{H_2O} + k_H[H^+] \quad (4)$$

Substituting the buffer-independent terms by k_0 and the buffer base and acid concentrations by $f_B[B]_T$ and $f_{HB}[B]_T$, where $[B]_T = [B] + [BH]$ and $f_B + f_{HB} = 1$, eq 4 yields

$$k_0 = k_{OH}[OH^-] + k_{H_2O} + k_H[H^+] \quad (5)$$

$$k_1 = \{k_B f_B + k_{HB}(1 - f_B)\}[B]_T + k_0 \quad (6)$$

$$k_1 = \{(k_B - k_{HB})f_B + k_{HB}\}[B]_T + k_0 \quad (7)$$

Inquiring further after the publication, we noted that in the hydrolysis of **4** (eq 2), the slope of k_1 vs. buffer concentration in the area of relatively basic buffers increased as the buffer basicity increased.[9] In other words, the plots of $(k_B - k_{HB})f_B + k_{HB}$ against f_B do not give a straight line with a slope $k_B - k_{HB}$ but an upward curvature in the basic area. Substantially the same observations were obtained in the present system. Therefore, the rate law may involve the term catalyzed by hydroxide and buffer ions, $k_{BT,OH}$-$[OH][B]_T$.

$$k_1 = \{k_B f_B + k_{HB}(1 - f_B) + k_{BT,OH}[OH^-]\}[B]_T + k_0 \quad (8)$$

$$k_1 = k'_{BT}[B]_T + k_0 \quad (9)$$

Plots of k_1 in Table I against total buffer concentrations $[B]_T$, when the ionic strength remained constant at a given pH, afforded satisfactory straight lines in all cases. Examples with the acetate buffer are shown in Figure 1. The linearity confirmed the expectation of eq 9 that k_1 depends on buffer concentration. The slope, k'_{BT}, and intercepts, k_0, of such plots are given in Table II. Figure 2 shows the dependence of the logarithms of the k_0 on pH. From eq 5 and Figure 2, the k_0 value in the area independent of pH is k_{H_2O}, 9.55 × 10^{-8} s^{-1}.

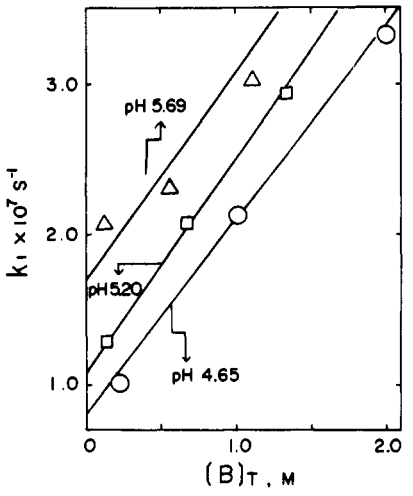


Figure 1. Effect of varying total acetate buffer concentration on the rate constant for the hydrolysis of **10** at several pH values, 25 °C, and μ = 1.0 M.

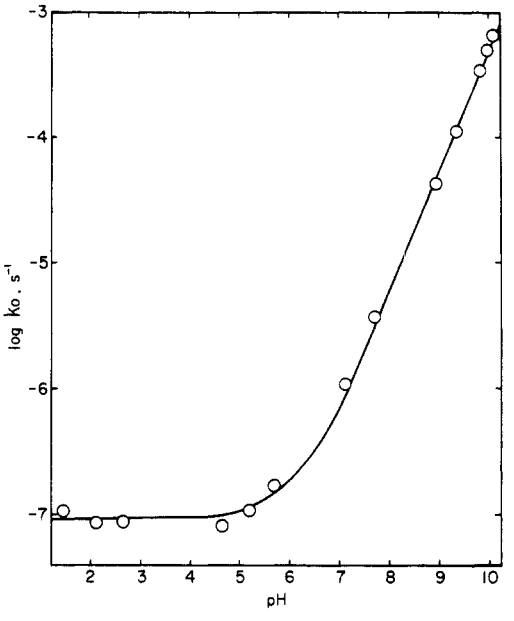


Figure 2. log k_0 vs. pH profile for the hydrolysis of **10** at zero buffer concentration, 25 °C, and μ = 1.0 M.

The large dependence of the k'_{BT} values on pH in the area of pH ≥8.94 in Table II permits the assumption in this area of $k_{BT,OH}[OH^-] \gg k_B f_B$ and $k_{HB}(1 - f_B)$. Thus, $k'_{BT} \simeq k_{BT,OH}[OH^-]$ and $\log k'_{BT} \simeq \log k_{BT,OH}[OH^-] = \log k_{BT,OH} + pH - pK_w$.

The assumption is validated by the fact that, when the log k'_{BT} values at the five highest pH values (8.94, 9.34, 9.81, 9.97, 10.10) in the carbonate buffer are plotted against pH on an appropriate scale, a straight line having a unit slope is obtained as shown in Figure 3.[10] Thus, we can derive $\log k_{BT,OH}[OH^-] = -4.35$ at pH 9, $k_{BT,OH}[OH^-] = 4.47 \times 10^{-5}$ M^{-1} s^{-1}, and $k_{BT,OH} = 4.44$ M^{-2} s^{-1}.

In the relatively acidic acetate buffer, the rate law is eq 4. Following the previous calculation[7]

$$k_1 = \{k_B + (k_{HB}/K'_a)[H^+]\}[B] + k_0 \quad (10)$$

(9) This fact and the general-acid-catalysis effects observed were noted by Professor R. L. Schowen in a private communication. We are very grateful to him.

(10) Of interest is the finding that the straight line in Figure 3 can be extrapolated for the log k'_{BT} at pH 7.70 in the phosphate buffer. The present data are not sufficient to clarify whether the finding is due to coincidence or the value of $k_{BT,OH}$ is independent of the nature of the buffer structure.

Table I. Rates for Hydrolyses of [(9-Oxobenzonorbornen-*exo*-2-yl)methyl]methyl(*p*-nitrophenyl)sulfonium Tetrafluoroborate (10)[a]

A. Acetate Buffer, CH_3COONa-CH_3COOH

pH	[B]/[BH][b]	$[B]_T$	k_{obsd}, s^{-1} 80.0 °C	k_{obsd}, s^{-1} 65.0 °C	$k_1^{25.0\,°C}$,[c] s^{-1}
4.65	1:1	2.0	$(2.37 \pm 0.01) \times 10^{-4}$	$(4.87 \pm 0.05) \times 10^{-5}$	3.32×10^{-7}
		1.0	$(1.72 \pm 0.02) \times 10^{-4}$	$(3.43 \pm 0.06) \times 10^{-5}$	2.13×10^{-7}
		0.2	$(1.19 \pm 0.03) \times 10^{-4}$	$(2.17 \pm 0.05) \times 10^{-5}$	1.02×10^{-7}
5.20	3:1	1.33	$(2.30 \pm 0.03) \times 10^{-4}$	$(4.62 \pm 0.08) \times 10^{-5}$	2.94×10^{-7}
		0.67	$(1.75 \pm 0.03) \times 10^{-4}$	$(3.45 \pm 0.03) \times 10^{-5}$	2.07×10^{-7}
		0.13	$(1.32 \pm 0.02) \times 10^{-4}$	$(2.48 \pm 0.08) \times 10^{-5}$	1.28×10^{-7}
5.69	9:1	1.11	$(3.21 \pm 0.12) \times 10^{-4}$	$(5.99 \pm 0.12) \times 10^{-5}$	3.02×10^{-7}
		0.56	$(2.33 \pm 0.06) \times 10^{-4}$	$(4.40 \pm 0.06) \times 10^{-5}$	2.30×10^{-7}
		0.11	$(1.81 \pm 0.08) \times 10^{-4}$	$(3.54 \pm 0.08) \times 10^{-5}$	2.07×10^{-7}

B. Phosphate Buffer, Na_2HPO_4-KH_2PO_4

pH	[B]/[BH][b]	$[B]_T$	k_{obsd}, s^{-1} 65.0 °C	k_{obsd}, s^{-1} 50.0 °C	$k_1^{25.0\,°C}$,[c] s^{-1}
7.12	3:1	0.3	$(3.59 \pm 0.05) \times 10^{-4}$	$(5.71 \pm 0.12) \times 10^{-5}$	1.78×10^{-6}
		0.15	$(3.15 \pm 0.05) \times 10^{-4}$	$(4.93 \pm 0.11) \times 10^{-5}$	1.49×10^{-6}
		0.03	$(2.59 \pm 0.05) \times 10^{-4}$	$(3.95 \pm 0.08) \times 10^{-5}$	1.14×10^{-6}

pH	[B]/[BH][b]	$[B]_T$	k_{obsd}, s^{-1} 50.0 °C	k_{obsd}, s^{-1} 35.0 °C	$k_1^{25.0\,°C}$,[c] s^{-1}
7.70	9:1	0.3	$(1.59 \pm 0.02) \times 10^{-4}$	$(2.02 \pm 0.01) \times 10^{-5}$	4.56×10^{-6}
		0.15	$(1.46 \pm 0.03) \times 10^{-4}$	$(1.84 \pm 0.02) \times 10^{-5}$	4.13×10^{-6}
		0.03	$(1.37 \pm 0.02) \times 10^{-4}$	$(1.71 \pm 0.02) \times 10^{-5}$	3.81×10^{-6}

C. Carbonate Buffer, Na_2CO_3-$NaHCO_3$

pH	[B]/[BH][b]	$[B]_T$	$k_{obsd}^{25.0\,°C}$, s^{-1}
8.94	1:9	0.30	$(5.32 \pm 0.07) \times 10^{-5}$
		0.21	$(5.04 \pm 0.05) \times 10^{-5}$
		0.12	$(4.74 \pm 0.05) \times 10^{-5}$
		0.03	$(4.34 \pm 0.04) \times 10^{-5}$
9.34	1:3	0.30	$(1.43 \pm 0.01) \times 10^{-4}$
		0.21	$(1.36 \pm 0.01) \times 10^{-4}$
		0.12	$(1.25 \pm 0.003) \times 10^{-4}$
		0.03	$(1.14 \pm 0.01) \times 10^{-4}$
9.81	1:1	0.30	$(4.03 \pm 0.02) \times 10^{-4}$
		0.21	$(3.72 \pm 0.02) \times 10^{-4}$
		0.12	$(3.69 \pm 0.01) \times 10^{-4}$
		0.03	$(3.41 \pm 0.01) \times 10^{-4}$
9.97	3:2	0.30	$(5.96 \pm 0.06) \times 10^{-4}$
		0.21	$(5.51 \pm 0.07) \times 10^{-4}$
		0.12	$(5.38 \pm 0.02) \times 10^{-4}$
		0.03	$(4.99 \pm 0.02) \times 10^{-4}$
10.10	2:1	0.30	$(8.44 \pm 0.07) \times 10^{-4}$
		0.21	$(8.04 \pm 0.06) \times 10^{-4}$
		0.12	$(7.29 \pm 0.03) \times 10^{-4}$
		0.03	$(6.80 \pm 0.06) \times 10^{-4}$

D. NaOH-Citric Acid Buffer

pH	[B]/[BH][b]	$[B]_T$	k_{obsd}, s^{-1} 100.0 °C	k_{obsd}, s^{-1} 80.0 °C	$k_1^{25.0\,°C}$,[c] s^{-1}
2.70	1:2	2.0	$(7.77 \pm 0.33) \times 10^{-4}$	$(1.13 \pm 0.02) \times 10^{-4}$	1.51×10^{-7}
		1.0	$(7.82 \pm 0.40) \times 10^{-4}$	$(1.10 \pm 0.03) \times 10^{-4}$	1.31×10^{-7}
		0.2	$(8.60 \pm 0.28) \times 10^{-4}$	$(1.10 \pm 0.01) \times 10^{-4}$	9.47×10^{-8}

E. HCl Buffer

pH	[HCl], M	k_{obsd}, s^{-1} 100.0 °C	k_{obsd}, s^{-1} 80.0 °C	k_{obsd}, s^{-1} 65.0 °C	$k_1^{25.0\,°C}$,[c] s^{-1}
1.50	0.05	$(8.41 \pm 0.09) \times 10^{-4}$	$(1.13 \pm 0.03) \times 10^{-4}$	$(2.08 \pm 0.03) \times 10^{-5}$	1.07×10^{-7}
2.14	0.01	$(9.71 \pm 0.32) \times 10^{-4}$	$(1.10 \pm 0.05) \times 10^{-4}$	$(2.11 \pm 0.03) \times 10^{-5}$	8.63×10^{-8}

[a] μ = 1.0 M with KCl, pH at 26 °C. [b] [B], [BH], and $[B]_T$ are molar concentrations of base, acid, and total buffer, respectively. [c] Extrapolated by a FACOM computer except for rates determined in the carbonate buffer.

where the K'_a is the dissociation constant of acetic acid, 1.753×10^{-5} at 25.0 °C. Plots of k_1 in Table I against acetate ion concentration for three different pH values give the slopes $k_B + (k_{HB}/K'_a)[H^+]$. Then, plots of these slopes vs. the hydrogen ion concentrations, $[H^+]$, for the three given pH values permit the evaluation of k_{HB} (here, k_{CH_3COOH}) = 1.26×10^{-7} M^{-1} s^{-1} and k_B ($k_{CH_3COO^-}$) = 1.20×10^{-7} M^{-1} s^{-1}.

As inspection of the k_0 values in Table II indicates that the $k_H[H^+]$ contribution to k_0 is absent, a plot of k_0 against

Table II. Dependence of k_0[a] and k'_{BT} (Eq 7)[b] on pH at 25.0 °C

pH	$[H^+]$[c]	$[OH^-]$[c]	$10^7 k_0$, s^{-1}	$10^7 k'_{BT}$, M^{-1} s^{-1}
1.50	3.16×10^{-2}		1.07	
2.14	7.24×10^{-3}		0.863	
2.70	2.00×10^{-3}		0.878	1.09
4.65	2.24×10^{-5}	4.50×10^{-10}	0.810	1.29
5.20	6.31×10^{-6}	1.60×10^{-9}	1.08	1.43
5.69	2.04×10^{-6}	4.93×10^{-9}	1.70	1.39
7.12	7.59×10^{-8}	1.33×10^{-7}	10.6	26.0
7.70	2.00×10^{-8}	5.05×10^{-7}	37.3	27.7
8.94		8.77×10^{-6}	428	370
9.34		2.20×10^{-5}	1120	1093
9.81		6.50×10^{-5}	3360	2147
9.97		9.40×10^{-5}	4930	3203
10.10		1.27×10^{-4}	6560	6533

[a] Rate constant at zero concentration of buffer. [b] Slopes in Figure 1. [c] $[H^+] = 10^{-pH}$, $\log [OH^-] = pH - pK_w$.

the hydroxyl ion concentration, $[OH^-]$ [$\log [OH^-] = (pK_w - pH)$], as shown in Figure 4, permits evaluation of the slope, k_{OH}, and the intercept, k_{H_2O}. Since the pK_w of water at 25.0 °C is 13.997, the treatment gives $k_{OH} = 5.18$ M^{-1} s^{-1}.

A solvent isotope effect was determined for the reaction of **10** in deuterium oxide buffered with acetic acid–sodium acetate. The data are listed in Table III and extrapolations of k_{obsd} to zero buffer concentration give $k_{D_2O} = 1.98 \times 10^{-5}$ s^{-1} at 65.0 °C and 1.07×10^{-4} s^{-1} at 80.0 °C. Since k_{H_2O} is derived from Table I as 2.25×10^{-5} s^{-1} at 65.0 °C and 1.21×10^{-4} s^{-1} at 80.0 °C, the ratio k_{H_2O}/k_{D_2O} is 1.14 at 65.0 °C and 1.13 at 80.0 °C.

As a reference compound, the epimeric [(9-oxobenzonorbornen-*endo*-2-yl)methyl]methyl(*p*-nitrophenyl)sulfonium tetrafluoroborate (**11**) was hydrolyzed in acetate buffer under the following conditions: pH 4.65, $[CH_3COONa]/[CH_3COOH]$ = 1:1, $[CH_3COONa]$ = 1.0 M (μ = 1.0 M). The reaction proceeded with a rate constant of $k_{obsd} = 2.66 \times 10^{-5}$ s^{-1} at 75.0 °C, which is the same rate as that of [(*anti*-9-hydroxybenzonorbornen-*endo*-2-yl)methyl]methyl(*p*-nitrophenyl)sulfonium tetrafluoroborate within experimental error.[7] As the product was **13** as mentioned above, the reaction pattern totally differed from that of the exo compound **10**.

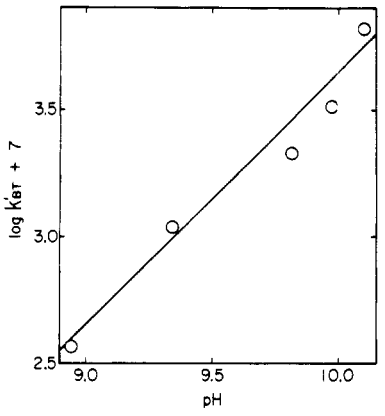


Figure 3. Dependence on pH (≥8.94) of the logarithm of the total buffer catalytic constant, k'_{BT}, at 25 °C and μ = 1.0 M.

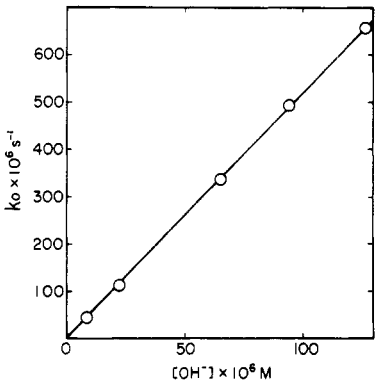


Figure 4. Dependence on hydroxyl ion concentration of the rate constant for the hydrolysis of **10** at zero buffer concentration, 25 °C, and μ = 1.0 M.

Discussion

Intermolecular nucleophilic attack on sulfonium compounds takes place only under forced conditions and such a water attack is exceedingly slow. Simple models for the present sulfonium compound **10** may be dimethyl(*p*-nitrophenyl)sulfonium perchlorate (**14**) and isobutylmethyl(*p*-nitrophenyl)sulfonium perchlorate (**15**). The

Table III. Rates of 10 in D_2O Buffered with CH_3COOD-CH_3COONa[a]

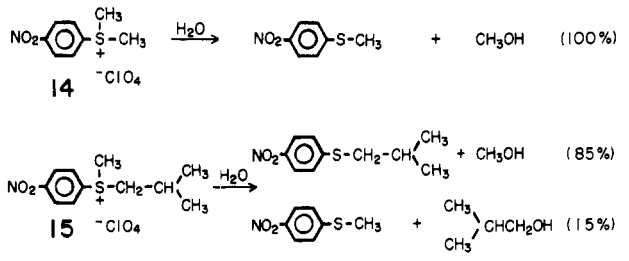
pH[b]	[B]/[BH]	$[B]_T$	k_{obsd},[c] s^{-1} 80.0 °C	k_{obsd},[c] s^{-1} 65.0 °C
5.2	1:1	1.0	$(2.14 \pm 0.03) \times 10^{-4}$	$(4.31 \pm 0.11) \times 10^{-5}$
		0.5	$(1.64 \pm 0.04) \times 10^{-4}$	$(3.03 \pm 0.12) \times 10^{-5}$
		0.1	$(1.18 \pm 0.07) \times 10^{-4}$	$(2.23 \pm 0.06) \times 10^{-5}$

[a] μ = 1.0 M with KCl, pH at 25 °C. [b] For determination of pH in D_2O refer to: Funk, M. O.; Kaiser, E. T. *J. Am. Chem. Soc.* **1977**, *99*, 5336-40 and ref 29 cited therein. [c] Plots of k_{obsd} vs. $[CH_3COO^-]$ give, at zero buffer concentration, $k_{D_2O} = 1.98 \times 10^{-5}$ s^{-1} at 65 °C and 1.07×10^{-4} s^{-1} at 80 °C. The treatments of k_{obsd} in Table I give $k_{H_2O} = 2.25 \times 10^{-5}$ s^{-1} at 65 °C and 1.21×10^{-4} s^{-1} at 80 °C.

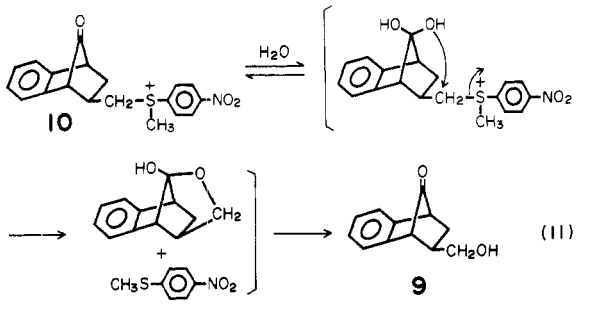
Table IV. Rates of Dimethyl(*p*-nitrophenyl)sulfonium Perchlorate (14) in CH_3COONa-CH_3COOH Buffer[a]

pH	[B]/[BH]	$[B]_T$	k_{obsd},[b] s^{-1} 80.0 °C	k_{obsd},[b] s^{-1} 100.0 °C	$k_1^{25.0\,°C}$,[c] s^{-1}
4.50	1:1	2.0	$(5.11 \pm 0.08) \times 10^{-5}$	$(4.40 \pm 0.09) \times 10^{-4}$	3.16×10^{-8}
		1.0	$(1.91 \pm 0.03) \times 10^{-5}$	$(1.65 \pm 0.02) \times 10^{-4}$	1.17×10^{-8}
pH	[B]/[BH]	$[B]_T$	k_{obsd},[b] s^{-1} 100.0 °C	k_{obsd},[b] s^{-1} 120.0 °C	$k_1^{25.0\,°C}$,[c] s^{-1}
4.50	1:1	0.2	$(3.63 \pm 0.05) \times 10^{-5}$	$(2.55 \pm 0.02) \times 10^{-4}$	2.44×10^{-9}

[a] μ = 1.0 M with $NaClO_4$, pH at 26 °C. [b] Extrapolation gives $k_{obsd} = 2.87 \times 10^{-5}$ at 75.0 °C and $[CH_3COO^-]$ = 1.0 M. [c] Plots of k_1 vs. $[CH_3COO^-]$ give $k_0 = 4 \times 10^{-10}$ s^{-1} at 25 °C at zero buffer concentration.



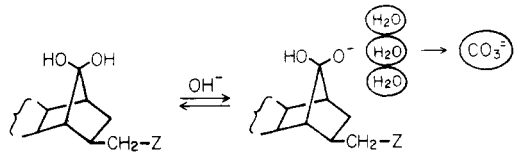
second-order rate constant of **14** with H_2O was roughly calculated as $\sim 10^{-11}$ M^{-1} s^{-1} in previous papers.[6,7] This time we determined the rate for the hydrolysis of **14** in CH_3COONa–CH_3COOH buffer at pH 4.50 under conditions similar to those employed for **10**, at a constant ionic strength (μ = 1 M with $NaClO_4$). The results are listed in Table IV and extrapolation of k_1 to the zero buffer concentration gives $k_0 = 4 \times 10^{-10}$ s^{-1}, which is considered to be the rate constant in an area independent of pH. Therefore, k_0 for **10** is 240 times greater than that for **14** and the effective molarity (EM) is derived as $9.55 \times 10^{-8}/(4 \times 10^{-10}/55.5) = 1.3 \times 10^4$ M. The hydrolysis of **15** in the acetate buffer was found to proceed with the formation of isobutyl *p*-nitrophenyl sulfide and *p*-nitro(methylthio)benzene in an 85:15 ratio. Thus, predominant nucleophilic attack occurs at the methyl carbon and not at the isobutyl secondary carbon which is sterically more hindered. Therefore, the highly effective rate and the exclusive attack at the secondary carbon observed for the hydrolysis of **10** suggest involvement of a special factor. On the other hand, the reaction of the endo isomer **11** is normal. The nucleophilic attack takes place at the less hindered methyl carbon, and the rate presented in the calculations is comparable to that of **14** in Table IV when determined under comparable conditions. We propose a participation mechanism by the 9-oxo group for the reaction of **10**, which is similar to the mechanism proposed for the solvolysis of **6** in aqueous solvent (eq 3).[8] Thus, the keto group is converted into a intermediate diol upon addition of a water molecule, and one of the hydroxyl groups formed participates in the transition state of the substitution reaction leading to an intramolecularly cyclized hemiketal intermediate (a five-membered ring), which is decomposed to the alcohol **9** in an aqueous medium (eq 11). Participation of this type is geometrically



(11)

impossible for the endo compound **11**. The participation of the hydroxyl oxygen in the hemiketal formation step is the same as in the hydrolysis of the 9-hydroxyl compound (**4**) (eq 2). Indeed, all the rate constants presented in the calculations are of almost the same order of magnitude as those recently reported for **4**.[7] Analogous types of carbonyl participation have been known in the hydrolysis of esters,[11] the reaction center of which is at the sp²-hybridized carbon atom, and, quite recently, in the solvolysis of a bromobenzenesulfonate[8] but not (to the best of our knowledge) in an S_N2 reaction such as the present one. As predicted by this mechanism, the hydrolysis of **10** is very sensitive to the hydroxide concentration, so that the k_{OH} (=5.18 M^{-1} s^{-1}) for **10** is 10^6 times greater than that ($\sim 10^{-6}$ M^{-1} s^{-1}) estimated for **14**.[7] Evidence for general-acid and -base-catalysis effects was shown in the acetate buffer medium: $k_{CH_3COOH} = 1.26 \times 10^{-7}$ M^{-1} s^{-1} and $k_{CH_3COO^-} = 1.20 \times 10^{-7}$ M^{-1} s^{-1} (25.0 °C).

Of particular interest is the evidence of catalysis effects by hydroxide ion and buffer ion: $k_{BT,OH} = 4.44$ M^{-2} s^{-1} at 25 °C in the carbonate buffer. In other words, the rate dependence on buffer concentration increases as the concentration of hydroxide ion increases. Hydration of carbonyl compounds is, in general, catalyzed by base,[12] so that increasing hydroxide ion concentration favors conversion of the keto group in the diol (eq 11) and facilitates formation of the diol anion (hydrate anion, $HO(O^-)C<$) which involves a reactive nucleophile hydroxide ion. We consider that the buffer ions affect solvation of the diol anion.



Water molecules surrounding the anion are attracted to the charge of buffer ions, e.g., carbonate ions. Thus, the anion becomes more desolvated, naked, and reactive.

Experimental Section

Melting points were taken in capillary tubes and are corrected. Infrared spectra were determined with a 215 Hitachi grating infrared spectrophotometer, ^1H NMR spectra with a Varian T-60A, and ultraviolet spectra with an EPS-3T Hitachi recording spectrophotometer.

[(9-Oxobenzonorbornen-*exo*-2-yl)methyl]methyl(*p*-nitrophenyl)sulfonium Tetrafluoroborate (10). To a stirred solution of 214 mg of silver tetrafluoroborate in 4 mL of nitromethane were added, at room temperature, a solution of 325 mg of the sulfide **12**[7] in 5 mL of nitromethane and a solution of 780 mg of methyl iodide in 4 mL of nitromethane. The mixture was stirred for 3 h and the yellow-white crystals which precipitated were removed by filtration. The filtrate was concentrated under reduced pressure, leaving an oil which was treated with chloroform and methylene chloride to afford 369 mg of yellow crystals: mp 189 °C dec (from acetonitrile–ether); IR (Nujol) 1780 cm^{-1} (CO); NMR (Me_2SO-d_6) δ 1.7–2.4 (m, 3, at C_2C_3), 3.4–3.6 (overlapping m, 2, at C_1C_4), 3.5 (s, 3, S^+CH_3), 4.1 (m, 2, CH_2S^+), 7.4 (4, aromatic), 8.5 (4, aromatic). Anal. Calcd for $C_{19}H_{18}NO_3SBF_4$: C, 53.41; H, 4.25; N, 3.28; S, 7.50. Found: C, 53.14; H, 4.27; N, 3.39; S, 7.75. The endo epimer **11** was similarly prepared from the reported sulfide **13**[7] and used for kinetic studies without purification.

Hydrolysis Products. The reaction mixture obtained on hydrolysis of **10** in an acetate buffer medium was extracted with ether. The ether solution was dried and evaporated. Preparative layer chromatography of the residual oil afforded *p*-nitro(methylthio)benzene and the keto alcohol **9**, which was recently reported.[8]

The workup procedure afforded the sulfide **13** on hydrolysis of **11** in an acetate buffer medium ($[CH_3COO^-]/[CH_3COOH]$ = 1:1, μ = 1.0 M) at 75 °C. The absence of *p*-nitro(methylthio)benzene in the products was confirmed.

Hydrolysis Rates as Functions of pH and Buffer Concentrations. Hydrolysis studies of **10** were conducted at 1×10^{-4} M in the given buffer system[13] and are summarized in Table I.

(11) Bender, M. L.; Silver, M. S. *J. Am. Chem. Soc.* **1962**, *84*, 4589–90. Bender, M. L.; Reinstein, J. A.; Silver, M. S.; Mikulak, R. *Ibid.* **1965**, *87*, 4545–53 and references cited therein. Kemp, K. C.; Mieth, M. L. *Chem. Commun.* **1969**, 1260–1. Bowden, K.; Taylor, G. R. *Ibid.* **1967**, 1112–3.

(12) For example, see: Carey, F. A.; Sundberg, R. J. "Advanced Organic Chemistry, Part A"; Plenum Press: New York, 1977; pp 326–8.

Portions were removed at various times and subjected to spectrometric analysis at the UV maximum at 350 nm to measure the *p*-nitro(methylthio)benzene being formed. Although the portions were homogeneous solutions during the reactions, they were not during the UV spectral measurements at room temperature because the products were not sufficiently soluble in the buffer media at such a low temperature. Thus, acetonitrile was added to make the solutions homogeneous during measurement. The difference between absorption intensities at infinite time and a specified time indicated the amount of remaining **10**. Thus, the pseudo-first-order rate coefficients were calculated with a FACOM computer.

(13) Refer to: Perrin, D. D.; Dempsey, B. "Buffers for pH and Metal Ion Control"; Chapman and Hall: London, 1974.

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Registry No. 9, 70969-20-9; **10**, 73198-19-3; **11**, 73245-78-0; **12**, 68258-55-9; **13**, 68330-66-5; **14**, 29843-53-6; **15**, 73198-21-7.

Enones with Strained Double Bonds. 4. The Bicyclo[5.3.1]undecane System[1]

Herbert O. House,* Ronald F. Sieloff, Thomas V. Lee, and Marvin B. DeTar

School of Chemistry, Georgia Institute of Technology, Atlanta, Georgia 30332

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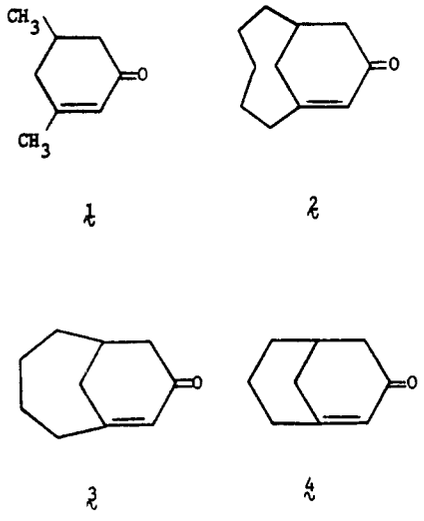
Bicyclo[5.3.1]undec-7-en-9-one (**2**) has been synthesized from cyclooctenone. This bicyclo[5.3.1] enone system **2** shows less tendency to add nucleophiles in a conjugate manner than is the case for the more strained bicyclo[4.3.1] enone **3** and bicyclo[3.3.1] enone **4**. Comparison of the ultraviolet spectra and the electrochemical reduction potentials of the monocyclic enone **1** and the bicyclic enones **2** and **3** indicates that these compounds absorb light at longer wavelengths and that they are more easily reduced to the corresponding anion radicals as distortion of the conjugated enone system increases. Force field calculations have been used to estimate the degree of distortion present in the enone systems of these bicyclic compounds.

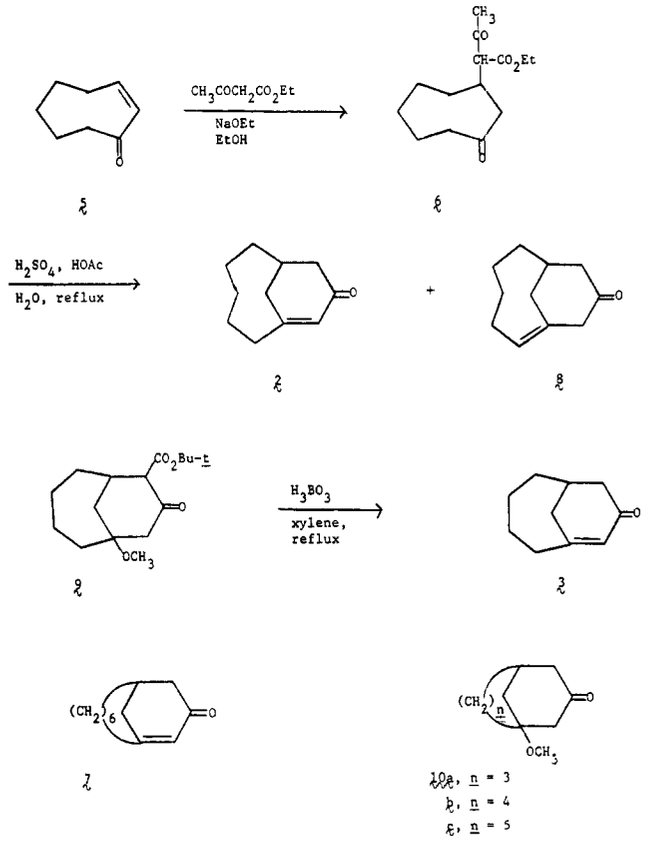
In continuing our study of enones with strained double bonds,[2] we wished to compare the properties of the series of enones **1**–**4**. In this series the distortion of the C=C



bond was expected to vary from essentially none (enone **1**) to substantial twisting in the enone **4**[2a,c] whose high reactivity has thus far prevented isolation. This paper reports the synthesis of the bicyclic enone **2** and compares certain of the chemical and physical properties of the series of enones **1**–**4**.

The synthesis of the enone **2** was accomplished by the Michael addition of ethyl acetoacetate to cyclooctenone (**5**, Scheme I) followed by treatment of the adduct **6** with

Scheme I



a refluxing mixture of H_2SO_4, HOAc, and H_2O. This synthesis, which is analogous to the method used earlier for the formation of the larger bicyclic enone **7**,[3] initially formed a mixture of the conjugated enone **2** and the un-

(1) This research has been supported by Public Health Service Grant R01-GM-20197 from the National Institute of General Medical Science. The exceution of this research was also assisted by Institutional Research grants from the National Science Foundation for the purchase of a mass spectrometer and a Fourier transform NMR spectrometer.

(2) (a) House, H. O.; Kleschick, W. A.; Zaiko, E. J. *J. Org. Chem.* **1978**, *43*, 3653. (b) House, H. O.; Lee, T. V. *Ibid.* **1979**, *44*, 2819. (c) House, H. O.; DeTar, M. B.; VanDerveer, D. *Ibid.* **1979**, *44*, 3793.

(3) Gioia, B.; Marchesini, A.; Andreeti, G. D.; Bocelli, G.; Sgarabotto, P. *J. Chem. Soc., Perkin Trans. 1* **1977**, 410.

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