CHEMISTRY LETTERS, pp. 1063-1066, 1980.

β-CYCLODEXTRIN PHOSPHATE. A REMARKABLE CATALYST FOR THE IODINE OXIDATION OF BENZYL METHYL SULFIDE TO THE SULFOXIDE IN WATER

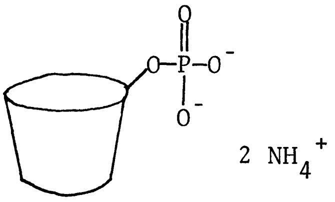
Toshio EIKI and Waichiro TAGAKI*
Department of Chemistry, Faculty of Engineering, Gunma University, Kiryu, Gunma;
*Department of Applied Chemistry, Faculty of Engineering,
Osaka City University, Sugimotocho, Sumiyoshiku Osaka

β-Cyclodextrin phosphate has been found to be a remarkable catalyst for the iodine oxidation of benzyl methyl sulfide to the sulfoxide in water.

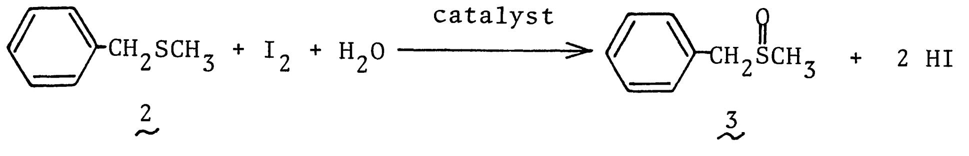
Modification of cyclodextrins (cycloamyloses) to obtain better enzyme models has been the subject of considerable interests in the past decade.[1)] Recently, Breslow and the coworkers reported the synthesis of isomeric monophosphates of β-cyclodextrin (β-CD) and examined their catalytic activities for acetal hydrolysis and enolization of ketones.[2)] This work has drawn our attention, because the phosphates might be much better catalyst for the title oxidation reaction[3)] than the catalyst of inorganic orthophosphate discovered a decade ago by Higuchi and Gensch.[4)] This possibility has now been confirmed to be real as described below.

The diammonium salt of β-CD monophosphate (1) was prepared by reacting bis-(m-nitrophenyl)phosphate with β-CD according to the essentially similar procedure described by Breslow et al.[2)] The product (1) was actually a mixture of two isomeric cycloheptaamylose 2-phosphate (minor) and 3-phosphate (major).[2)] Breslow et al separated these two isomers, but found their following properties to be almost the same: the values of pKa_1 and pKa_2; the binding ability to include an aromatic ketone into the amylose cavity (i.e. K_d); the catalytic rate constant (k_{cat}) for enolization. Therefore, the mixture (1) was used in this work without further separation into its components.

The rates of oxidation of benzyl methyl sulfide (2) (eq. 1) were followed by spectrophotometric measurement of the decrease of triiodide ion (286 nm) under the



1



(1)

catalyst: 1, $HPO_4^{=}$

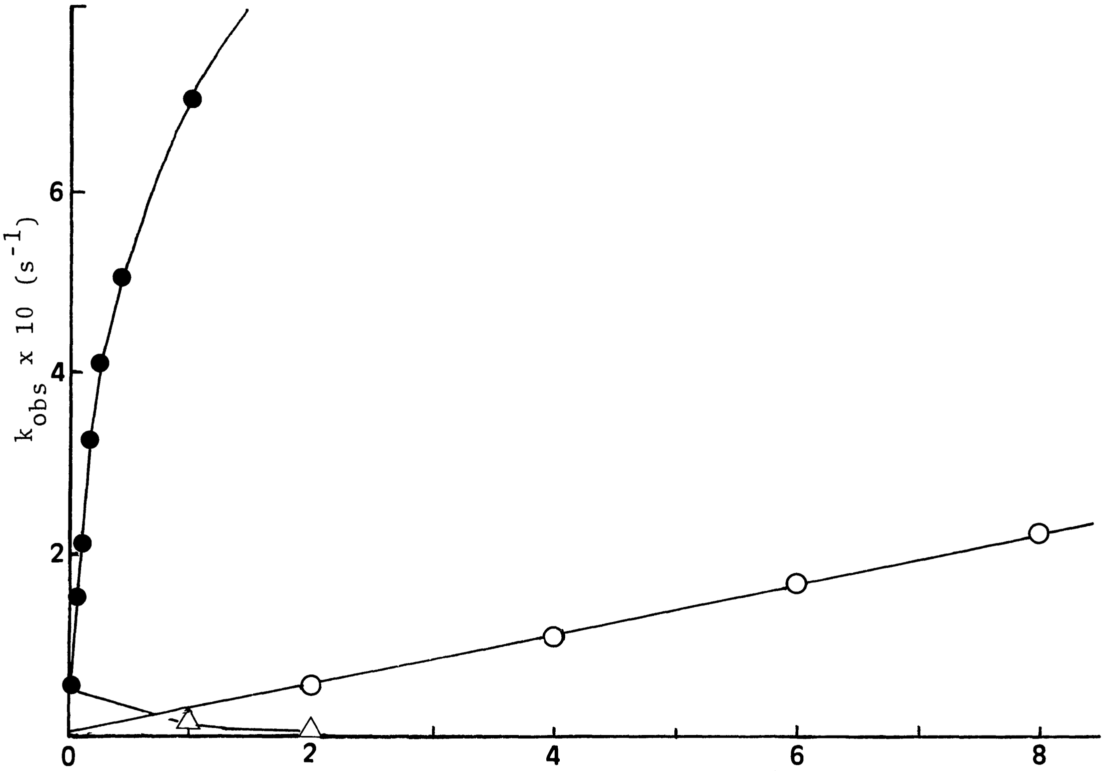


Fig. 1. Plots of pseudo-first-order rate constant(k_{obs}) against catalyst concentration in the iodine oxidation of benzyl methyl sulfide (2) at 25°C in aqueous buffer (pH 7.2) containing 5%(v/v) methanol: [2]=1.06×10^{-3}M; [I_2]=8.33×10^{-5}M, [KI]=3.32×10^{-4}M; ○, phosphate buffer; ●, 1 + 2×10^{-3}M phosphate buffer; △, β-CD + 2×10^{-3}M phosphate buffer.

conditions of an excess sulfide over iodine according to the method of Higuchi and Gensch.[4,5] The results are shown in Fig. 1. The linear plots for phosphate buffer give the buffer catalysis k_2(phosphate) as the slope of line which is similar in magnitude to that reported by Higuchi and Gensch.[4] The catalysis by **1** is much larger. Furthermore, the plots for **1** show saturation of rate which is consistent with the usual reaction scheme (eq. 2) for 1:1 complexation between the catalyst (C) and the substrate (S) and can be analyzed by the Lineweaver-Burk plot of eq. 3.[6] Unmodified intact β-CD inhibits the catalysis of phosphate buffer, presumably by binding the substrate and by separating it from the contact with phosphate catalyst. The results are shown in Table 1. The table indicates that **1** enhances the rate by 500 fold (k_o vs. k_{cat}) and is 35 fold more effective than inorganic orthophosphate ($k_{cat}K/k_2$(phosphate)). The association constant (K= 312 M^{-1})

$$\begin{tikzcd} C + S \arrow[r, shift left, "K"] \arrow[rr, bend right, "k_o'"'] & C\cdot S \arrow[l, shift left] \arrow[r, "k_{cat}"] & P \end{tikzcd} \qquad (2)$$

$$\frac{1}{(k_{obs} - k_o')} = \frac{1}{(k_{cat} - k_o')} + \frac{1}{(k_{cat} - k_o')}\cdot\frac{1}{K}\cdot\frac{1}{[C]_T} \qquad (3)$$

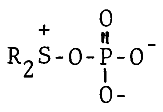
Table 1. Rate and Association Constants[a)]

Catalyst	k_o, k_{cat} (s^{-1})	k_2, $k_{cat}K$ (M^{-1} s^{-1})	K (M^{-1})
None	5.90×10^{-3} [b)]	-	-
Na_2HPO_4	-	26.2	-
1	2.93	915	312

(a) For the reaction conditions, see Fig. 1.

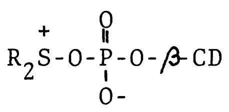
(b) Calculated value as the intercept of the linear plots for phosphate buffer in Fig. 1.

is an expected value for the complex of 2 and β-CD. The fact that 1 is more active than orthophosphate appears to be important, since 1 is the monoalkylphosphate and structurally different from orthophosphate. According to the mechanism proposed by Higuchi and Gensch,[4] the catalysis by orthophosphate proceeds through the rate determining decomposition of an intermediate dianion, 4. While in the case of 1, the corresponding intermediate should be the monoanion, 5. Further discussions are difficult at present, since the reaction involves complex equilibria depending on the concentration of substrate, reagents, pH, etc.



$R_2\overset{+}{S}-O-\underset{O^-}{\overset{\overset{O}{\|}}{P}}-O^-$

4



$R_2\overset{+}{S}-O-\underset{O^-}{\overset{\overset{O}{\|}}{P}}-O-\beta\text{-CD}$

5

Further studies such as on the substrate specificity and possible application for synthesis are now in progress in this laboratory.

This work was partially supported by a Grant-in-Aid for Scientific Research from the Ministry of Education, Japan.

References and Notes

(1) a) D. W. Griffiths and M. L. Bender, Advan. Cat., 1973, 23, 209;
b) M. L. Bender and M. Komiyama, "Cyclodextrin Chemistry", Springer, (1978).

(2) B. Siegel, A. Pinter, and R. Breslow, J. Am. Chem. Soc., 98, 2309 (1977).

(3) The catalytic oxidation of sulfide has been the subject of our continued interest: see, W. Tagaki, M. Ochiai, and S. Oae, Tetrahedron Letters, 6131 (1968).

(4) T. Higuchi and K. H. Gensch, J. Am. Chem. Soc., 88, 3874, 5486 (1966).

(5) Quantitative formation of product sulfoxide (3) was confirmed by high speed liquid chromatography.

(6) The scheme of eq. 2 gives an equation, $k_{obs}=(k_o' + k_{cat}K[C]_T)/(1 + K[C]_T)$, which can be rearranged to give eq. 3, where $k_o' = k_o + k_2$[orthophosphate], and k_o, k_2, k_{cat}, K, and $[C]_T$ are the pseudo-first-order rate constant in the absence of catalyst, the second order rate constant for the catalysis of inorganic orthophosphate, the catalytic rate constant for the complex, association constant for the complex, and the total concentration of catalyst, respectively.

(Received June 16, 1980)