62–65 °C). The peaks of visible absorption spectra of **5** appeared at 420, 515, 550, 593, and 650 nm. The nmr spectra of **5** showed peaks at (δ, $CDCl_3$) 0.88 (t, 3H, CH_3), 1.25 (s, 28H, CH_2), 7.6–8.4 (15H, phenyl hydrogen), 8.7–8.9 (6H, pyrrole β-proton), 9.3–9.5 (2H, pyrrole β-proton). (Anal. Calcd. for **5**($C_{53}H_{56}N_4$): C, 84.90; H, 7.53; N, 7.49, Found: C, 84.73; H, 7.56; N, 7.28%). The band of R_f = 0.69 was tetraphenylporphyrin (307 mg). The porphyrin derivative (**5**, 100 mg) was metallized by heating it with zinc acetate (400 mg) to boiling for 2 hrs. The complex was purified on TLC (silicagel 60GF, methylene:cyclohexane = 1:3). The yield of zinc porphyrin derivative (**6**) was 99 mg (mp 72–75 °C). This method is quite straightforward. The visible spectra of **6** showed that λ_{max} are 423, 551, 589 nm. The absorption band of porphyrin derivative (**5**) on 650 nm disappeared in the absorption spectra of zinc porphyrin derivative (**6**). The absorption of **6** on 551 and 589 nm is characteristic for zinc porphyrin compound[7]. (Anal. Calcd. for $C_{53}H_{54}N_4Zn$: C, 78.36; H, 6.69; N, 6.89. Found: C, 78.63; H, 6.68; N, 6.87%). Hexadecanal was prepared by oxidation of hexadecanol with CrO_3-pyridine complex.

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The Effect of Medium on the α-Effect (Part 2)

Ik-Hwan Um

Department of Chemistry, Ewha Womans University, Seoul 120-750

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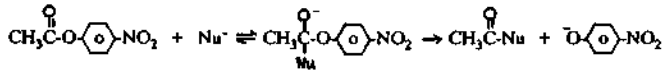
The term α-effect has been given to the enhanced nucleophilicity which is often observed in reactions of nucleophiles containing an atom with nonbonding electrons adjacent to the reaction center.[1] Numerous studies have been performed to explain the cause of the α-effect,[2] and the following have been most frequently suggested as the origin of the α-effect: destabilization of the ground-state,[3] stabilization of the transition-state,[4] intramolecular general acid-base catalysis,[5] polarizability,[1] and solvent effect.[6,7] However the origins for the α-effect are not completely understood yet. Particularly, the role of solvent on the α-effect has been the subject of controversy.[6,7]

Recently a systematic study has revealed that the α-effect is significantly dependent on solvent for the reactions of *p*-nitrophenyl acetate (PNPA) with butane-2,3-dione monoximate (1) as the α-nucleophile, in comparison with *p*-chlorophenoxide (2) as the corresponding normal-nucleophile in DMSO-H_2O mixed solvents.[8] A similar conclusion has also been drawn from the same reactions run in CH_3CN-H_2O mixtures of varying compositions.[9]

In order to investigate the role of solvent on the α-effect by an independent method, a series of reactions of PNPA with aryloxides and the oxymate (1) has been carried out in aqueous solutions of hexadecyltrimethyl ammonium bromide (CTAB).



Nu⁻ : $CH_3C(O)C(Me)=NO^-$ (1)

Such a bimolecular reaction causes usually significant rate enhancement, which is generally believed due to the result of bringing the two reactants together in a small volume of the surfactant aggregate.[10] Furthermore it has been very well known that the enhanced reactivity observed in reactions performed in aqueous CTAB solutions shows a good correlation with hydrophobicity of reactant.[11] Thus the present study would give us relative strength of solvation energy of the anionic nucleophiles in H_2O by investigating relative interaction between the reactants and surfactant aggregate.

The kinetic results for the reaction of PNPA with anionic nucleophiles in various concentrations of CTAB solutions are summarized in Table 1 and plotted in Figure 1. It is illustrated in Figure 1 that the reactivity increases sharply as the surfactant concentration increases up to a certain point as expected for the reactions of anionic nucleophiles in cationic surfactant solutions.[10] However the effect of CTAB on reactivity of *p*-$CNPhO^-$ is very small. The observed rate constants for *p*-$CNPhO^-$ in carbonate buffer solutions containing CTAB are almost identical to the one for carbonate buffer solution alone. This indicates that the contribution of *p*-$CNPhO^-$ to the observed rate constant is negligible, and such a low reactivity of *p*-$CNPhO^-$ could be attributed to the low basicity.

The rate enhancements for the other phenoxides are in the order of *p*-$EtPhO^-$ > *p*-$MePhO^-$ > *p*-$ClPhO^-$ > PhO^- in most region. Although the basicities of the three phenoxides except *p*-$ClPhO^-$ are very similar each other, their reactivities are very different in the presence of CTAB. Moreover, *p*-$ClPhO^-$ is generally more reactive in CTAB solutions than PhO^- although the former is less basic than the latter. This clearly indicates that basicity alone can not be a measure of nucleophilicity for the present system. Thus the Bronsted type of equation can not be used to correlate basicity with nucleophilicity for bimolecular reactions in presence of CTAB.

It has been reported that the interaction of phenoxides with surfactant aggregate decreases in the order of *p*-$EtPhO^-$ > *p*-$MePhO^-$ > PhO^-.[12] It is quite consistent with the present kinetic data, i.e. the phenoxide which interacts more strongly with CTAB shows more significant rate enhancement in CTAB solution or vice versa. Thus the higher rate enhance-

Table 1. Summary of Observed Rate Constants (min^{-1}) for the Reaction of PNPA with Various Phenoxides ($4\text{-X-}C_6H_4O^-$) and Butane-2,3-Dione Monoximate(Ox^-) in 0.025M Carbonate Buffer (pH 10.0) Containing Various Concentrations of CTAB at 25.0 °C

X	pK_a[c]	10^4[CTAB], M									
		0	4.0	6.0	10.0	14.0	20.0	26.0	36.0	48.0	60.0	76.0
C_2H_5	10.0	.120	.428	.590	.810	.936	1.09	1.20	1.30	1.29	1.29	1.29
CH_3	10.19	.124	.307	.433	.606	.756	.883	.954	1.09	1.13	1.18	1.19
H	9.95	.128	.208	.258	.350	.402	.486	.536	.618	.666	.678	.678
Cl	9.38	.125	.316	.403	.520	.579	.636	.666	.672	.684	.672	.666
		(.030)	(.139)	(.188)	(.257)	(.286)	(.292)	(.301)	(.311)	(.312)	(.312)	(.296)[b]
CN	7.95	.121	.135	.146	.164	.187	.202	.220	.241	.260	.280	.293
Ox^-	9.44	(.062)	(.684)	(1.31)	(2.42)	(3.26)	(4.25)	(5.13)	(5.95)	(6.42)	(6.85)	(6.96)[b]
carbonate	—	.115	.129	.140	.161	.187	.196	.208	.237	.258	.262	.287

[a][PNPA] = 1.0×10^{-5}M, [XC_6H_4OH] = 2.00×10^{-4}M. [b]The values in parentheses are the data in pH 9.2 borate buffer; [PNPA] = 1.0×10^{-5}M, [ClC_6H_4OH] = [OxH] = 1.00×10^{-4}M. [c]pKa values are taken from references 7c and 14.

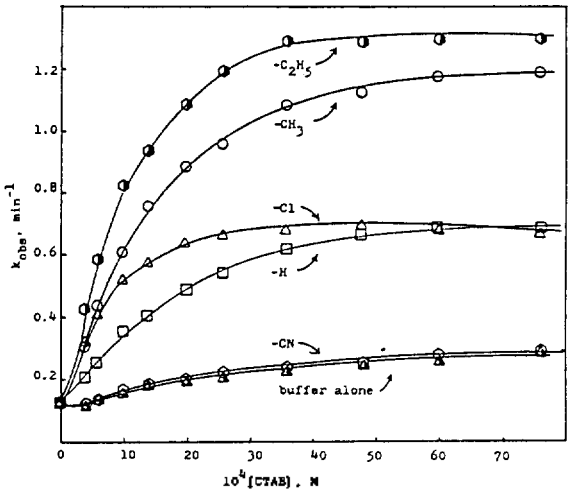


Figure 1. Plots of observed rate constants versus the concentration of CTAB for the reaction of PNPA with phenoxides ($4\text{-X-}C_6H_4O^-$) in 0.025M carbonate buffer (pH 10.0) at 25.0 °C.

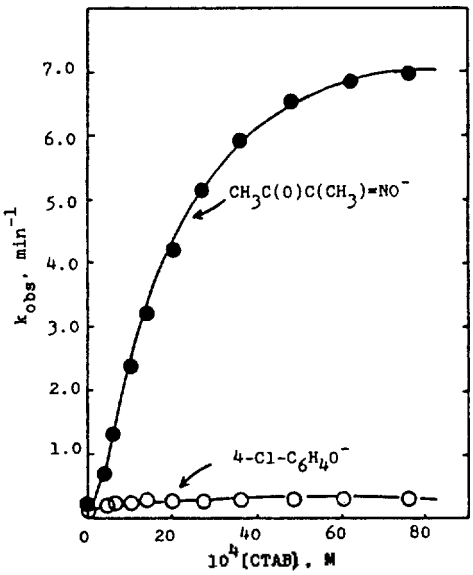


Figure 2. Plots of observed rate constants versus the concentration of CTAB for the reaction of PNPA with butane-2,3-dione monoximate and 4-chlorophenoxide in 0.1M borate buffer (pH 9.2) at 25.0 °C.

ment observed in the present system for p-$ClPhO^-$ than PhO^- seems to indicate that p-$ClPhO^-$ interacts more strongly with the CTAB aggregate than PhO^-. Therefore it is considered that nucleophilicity would be governed not only by the basicity of nucleophile but also by the strength of interaction between the nucleophile and CTAB aggregate, as expressed in equation (1),

$$\log k = a\log Ks + b\log Ka \quad (1)$$

where k, K_s and K_a represent nucleophilicity, strength of interaction between phenoxides and surfactant, and basicity of phenoxides, respectively. Similarly, a and b represent sensitivity parameter for K_s and K_a, respectively. Equation (1) would resemble the Bronsted type of equation when the first term approaches to zero. On the contrary when there is no pK_a difference between two nucleophiles, their reactivities in surfactant solutions would be mostly dependent on the magnitude of K_s, as happened in the present system.

In Figure 2 are plotted the observed rate constants versus CTAB concentrations for the reactions of PNPA with oximate (1) and p-$ClPhO^-$ (2) in pH 9.2 borate buffer solution. Interestingly the α-nucleophile (1) shows much more rate enhancement than the corresponding normal nucleophile (2) in all region of CTAB concentrations used. The present result clearly illustrates that the α-effect is present in aqueous CTAB solutions as well, and the magnitude of the α-effect increases with increasing CTAB concentration up to a certain point. Since the pK_a's of the conjugate acids of the two nucleophiles (1) and (2) are very similar, the difference in basicity of the two would not cause any significant differential rate acceleration upon the addition of CTAB to the reaction medium. Furthermore no mechanistic change is expected upon the environmental change of the reaction medium.[7d, 13] Therefore the differential rate enhancement between the two nucleophiles is considered to originate mainly from the difference in hydrophobicity of the two nucleophiles. The fact that the α-nucleophile shows much higher rate enhancement than the corresponding normal-nucleophile would lead the conclusion that the former is more hydrophobic and therefore, less strongly solvated in H_2O than the latter. This is consistent with the previous conclusions that the α-effect is significantly solvent depen-

dent.[8,9]

However more quantitative studies are required for a complete understanding of the present results. The calorimetric measurements of solution enthalpies of the reactants in various media are under way.

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A Novel Synthesis of Penems From Oxalimides

Jahyo Kang*, Weon Bin Im, Daesung Lim, Young Ro Choi, and Bong Young Chung*

Sogang University, Seoul 121-742
**Department of chemistry, Korea University, Seoul 136-701*

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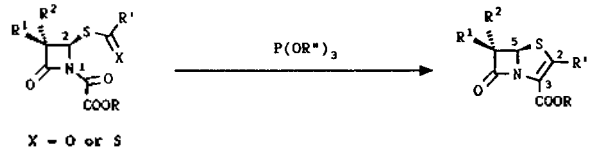
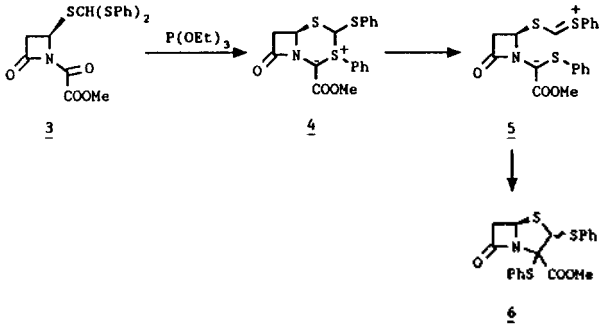
Methods for construction of the thiazoline rings in penems from preexisting azetidinones have been subjects of numerous studies[1] because of the emerging importance of this class of compounds as chemotherapeutic agents against bacteria. The reason for this is that the azetidinones are readily available by asymmetric synthesis, or by manipulation of cheap 6-aminopenicillanic acid and its derivatives. Among the thizoline-forming reactions, the phosphite-mediated reactions on 1-alkoxyoxalyl azetidinones **1** are used most widely[2]. And, this reaction is considered to proceed



1 **2**

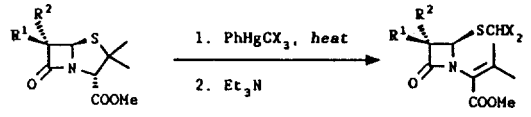
through an α-carboalkoxy carbene species, which is captured by phosphite to generate an ylide. Then, intramolecular olefination gives the penem **2**. The intervention of carbene species was further supported by Kametani *et al.* on the coupling reaction of 2-[di(alkylthio)methyl] azetidinone **3** by



3 **4** **5** **6**

triethyl phosphite to penam **6**, which was subsequently desulfurized by n-Bu_3SnH to the corresponding penem[2b].

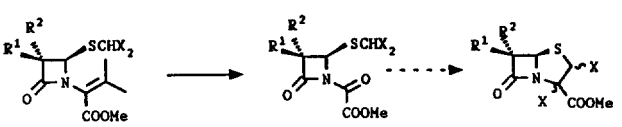
Recently, we have reported a novel C_2-S cleavage of penams by Seyferth reagent to give 4-dihalomethyl azetidinone **8**[3]. Since then, efforts were made to further function-



7 **8**

alize the C-4 dihalomethyl side chain in **8** and to prepare penems thereout. Although the former task was unsuccessful in our hand, this communication reports a new *direct* pathway to penems from oxalimides derived from ester **8**.

Consequently, ozonolysis of the α,β-unsaturated esters **8**[3] (CH_2Cl_2, -78 °C) followed by reductive work-up (Me_2S, -78 °C - 23 °C) provided the oxalimides **9** in nearly quantitative yields. Initially, it was thought that treatment of the oxalimides **9** with trialkyl phosphite would provide 2,3-dihalo penams **10** through the reaction path analogous to Eq. 2, which was not the case (*vide infra.*) (Eq. 4).



8 **9** **10**