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

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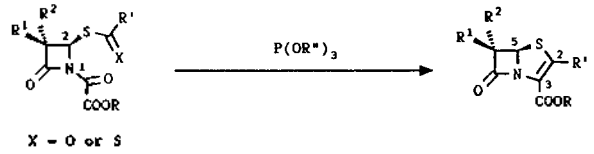
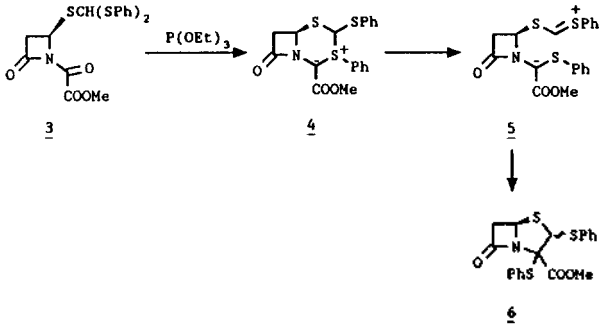
Methods for construction of the thiazoline rings in penems from preexisting azetidinones have been subjects of numerous studies[1] because of the emerging importance of this class of compounds as chemotherapeutic agents against bacteria. The reason for this is that the azetidinones are readily available 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**

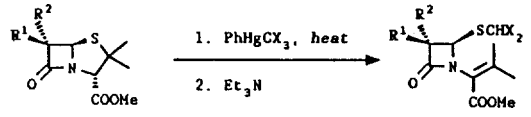
through an α-carboalkoxy carbene species, which is captured by phosphite to generate an ylide. Then, intramolecular olefination gives the penem **2**. The intervention of carbene species was further supported by Kametani *et al.* on the coupling reaction of 2-[di(alkylthio)methyl] azetidinone **3** by



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

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

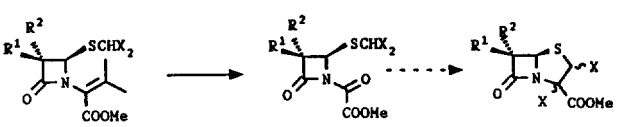
Recently, we have reported a novel C_2-S cleavage of penams by Seyferth reagent to give 4-dihalomethyl azetidinone **8**[3]. Since then, efforts were made to further function-



7 **8**

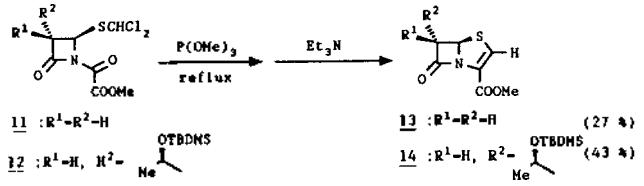
alize the C-4 dihalomethyl side chain in **8** and to prepare penems thereout. Although the former task was unsuccessful in our hand, this communication reports a new *direct* pathway to penems from oxalimides derived from ester **8**.

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).

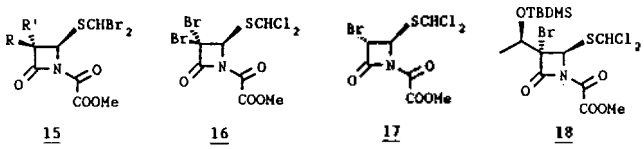


8 **9** **10**

Thus, heating of a solution of oxalimie **11** and $P(OMe)_3$ in toluene to reflux for 5 h generated two polar compounds, one minor (less polar) and major one (more polar), both of which were quite unstable enough to resist numerous attempts for isolation and characterization. However, treatment of the reaction mixture with an amine such as Et_3N or i-Pr_2NEt at rt for 12 h transformed the major one directly into methyl ester of the known penem **13**[4] devoid of chlorine, isolated in 27% yield after aqueous work-up and chromatography, which was rather surprising. The same behavior was noted for the silyloxyethyl oxalimide **12** (yield of **14**, 43%).

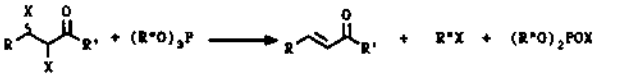


It was subsequently found that, understandably, 4-dibromomethylthio azetidinone oxalimides, **15**, regardless of substitution pattern at the C-3 position and those with halogen atom(s) at 3-position of the azetidinone ring, **16**–**18**, gave complex mitures under the same reaction condition. Also,



the phosphorus reagent for this reaction had to be specific: Among many phosphines and phosphites (PPh_3, $P(n\text{-}Bu)_3$, $P(OMe)_3$, $P(OEt)_3$, $P(OPh)_3$, $P(O\text{-}i\text{-}Pr)_3$, $P(OSiMe_3)_3$) examined so far, only trimethyl phosphite behaved properly.

Among the many possibilities, the mechanistic rationale at the moment may be outlined as described below: Initially, the oxalimide **9**(X = Cl) is converted to an α-alkoxycarbonyl carbene, which is eventually transformed into the 2,3-dichloropenam **10**(X = Cl) through the ensuing intermediacy of a chloronium ylide (analogous to **4**) and a 1,5-dipole (similar to **5**[2b]). Since trialkyl phosphite is known to dehalogenate α,β-dihalo carbonyl compounds (Eq. 6)[5], the dichloride **10** may well be reduced by trimethyl phosphite, eventually to



the corresponding penem. But the fact that the penems were not generated until the base treatment does suggest that the overall reaction occurred in a stepwise sense or the Perkow-type reaction somehow intervened during the process.

Regardless of the mechanistic details of the present reaction, herein is reported a new annulation of penem rings.

Acknowledgement. This work was generously supported by the Korea Science and Engineering Foundation.

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Rapid Ketonization of 2-Methylprop-1-en-1-ol in Chloroform: Reinvestigation of Stabilization with a Rhodium(I) Complex

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Kinetic studies for ketonization of enols have been carried out in aqueous solutions[1] as well as in some nonaqueous solvents.[2] But there has not been a report on kinetics for the ketonization in chloroform probably because it could not be clearly explained why the rate of ketonization in chloroform is unusually fast compared with those in H_2O[1] and in nonaqueous solvents.[1a,2] According to the mechanism suggested for ketonization of enols whose pK_a values are smaller than those of solvents (Eq. 1),[1,2] observed rate constants ($K_S \times k_{SH^+}$) are closely related with pK_a values of both solvents (S) and protonated solvents (SH^+).

$$R^1R^2C{=}C(OH)R^3 + S \overset{K_S}{\rightleftharpoons} R^1R^2C{=}C(O^-)R^3 + SH^+ \xrightarrow{k_{SH}^+} R^1R^2CHCOR^3 + S \quad (1)$$

The pK_a value of $CHCl_3$ (25)[3] is somewhat comparable with those of H_2O (15.7), CH_3OH (16), CH_3COCH_3 (20) and C_6H_6 (37)[4] and the ketonization is considerably slower in H_2O, CH_3OH, CD_3OD, CD_3COCD_3 and C_6D_6 than in $CDCl_3$.[2] (No