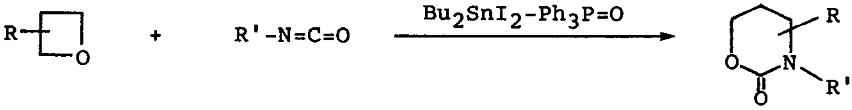
Tetrahedron Letters,Vol.26,No.42,pp 5167-5170,1985 0040-4039/85 $3.00 + .00
Printed in Great Britain

NOVEL USE OF ORGANOTIN HALIDE-BASE COMPLEX IN ORGANIC SYNTHESIS. CYCLOADDITION REACTION OF OXETANE WITH ISOCYANATES.

Akio Baba,* Ikuya Shibata, Masahiro Fujiwara and Haruo Matsuda
Department of Applied Chemistry, Faculty of Engineering,
Osaka University, Yamadaoka 2-1, Suita, Osaka 565, Japan

Summary: Cycloadditions of oxetanes with isocyanates were markedly accelerated by the complex of Bu_2SnI_2 and $Ph_3P{=}O$ which could be readily handled and hardly caused a trimerization of isocyanates, yielding oxazin-2-ones under neutral and mild reaction conditions.

Cycloadditions of heterocumulenes with oxiranes are conveniently used in the synthesis of five-membered heterocycles. Cycloadditions with oxetanes also would be useful method for preparations of six-membered heterocycles, if they should readily proceed. However, this type of cycloaddition has been less known perhaps because of the lower reactivity of oxetanes.[1] On the other hand, we recently reported some catalytic uses of organotin halide-bases complexes,[2] especially, alternate copolymerization of oxetane with carbon dioxide is caused by a unique catalytic action of organotin iodide-phosphine complexes.[3] Although many kinds of tin halide complexes have been reported,[4] the use in organic synthesis is limited. We describe here a new cycloaddition of oxetane with isocyanates by the complex of Bu_2SnI_2 and $Ph_3P{=}O$ (**3**), producing oxazin-2-ones (**4**) in good yields. This method has several advantages in terms of neutral and mild reaction conditions, and stability of the catalyst. To our knowledge, no study on this direct cycloaddition has been reported, perhaps for the reason of facile trimerization of isocyanates by usual catalyst for cycloadditions of oxiranes with isocyanates.[5] In this tin system the trimerization can be negligible in almost cases.



1 **2** **3** **4**

The method is illustrated by the following example. A mixture of dibutyltin diiodide (5 mmol), triphenylphosphine oxide (5 mmol), and oxetane (15 mmol) was stirred for 30 min at room temperature. Then, phenyl isocyanate (5mmol) was added and the mixture was heated at 40°C for 3h. After removing of unreacted oxetane in vacuo, the residue was subjected to silica gel column chromatography, yielding 3-phenyl-1,3-oxazin-2-one (**4a**) in 69% yield (eluted by $CHCl_3$).[6]

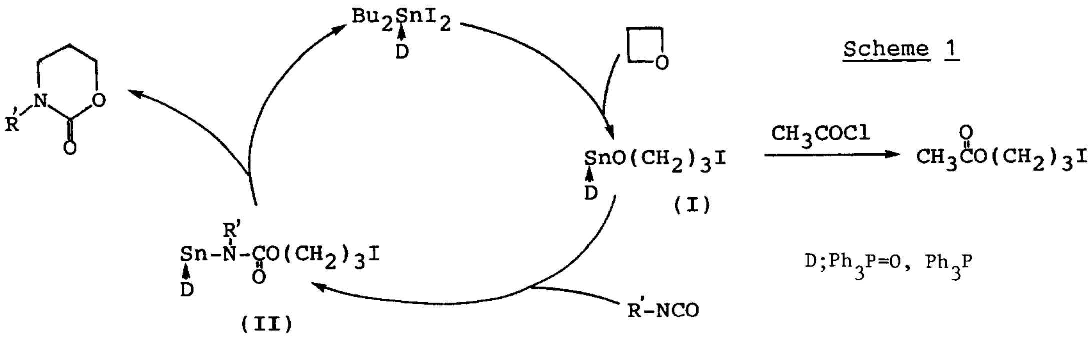
The reaction of oxetane with phenyl isocyanate proceeded even at room temperature in the presence of Bu_2SnI_2-base. The addition of bases in critical in this reaction since no consumption of phenyl isocyanate was occured in the case of using Bu_2SnI_2 alone, being determined by GLC and IR. As shown in Table 1, dibutyltin diiodide-base complexes have characteristic activity, whereas Bu_3SnI complex is less active which is the most effective catalyst for copolymerization of oxetane with carbon dioxide.[3]

Table 1. Synthesis of Oxazinone **4a** by Organotin Halide-Base Complexes[a]

Sn Halide	Base	Yield (%)
Bu_2SnI_2	$Ph_3P=O$	69
Bu_2SnI_2	Ph_3P	37
Bu_2SnBr_2	$Ph_3P=O$	0
Bu_3SnI	$Ph_3P=O$	19
Bu_3SnI	Ph_3P	trace
Bu_2SnI_2	-	0
Bu_2SnI_2[b]	Ph_3P	9 (81)[c]
Bu_2SnI_2[b]	$Ph_3P=O$	15 (85)[c]

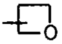
[a]Conditions; 40°C, 3h. [b]20°C, 3h. [c]Yield of $PhNHCOO(CH_2)_3I$.

In particular, it is noteworthy that $Ph_3P=O$ is more active than the corresponding base Ph_3P, giving **4a** in 69% and 37% yields, respectively. The basicity of $Ph_3P=O$ is so low that the trimerization of isocyanates would hardly occur in contrast with typical Lewis bases such as tertiary phosphines,[7] even if the complexation with $Ph_3P=O$ was incomplete. Moreover, these tin halides and phosphine oxide are very stable, and can be readily handled in air without any special techniques. By using **3**, a variety of oxazinones was successfully synthesized from the cycloaddition of oxetanes and isocyanates as shown in



Scheme 1

D; $Ph_3P=O$, Ph_3P

Table 2. Reactions of Oxetanes (R-) and R'-NCO by the Complex **3**[a]

Entry	R	R'	Temp (°C)	Oxazinone	Yield (%)	m.p. (°C)
1	H	Ph	40	**4a**	69	97-99
2	H	*p*-MeC_6H_4	40	**4b**	78	127
3	H	*p*-ClC_6H_4	40	**4c**	66	88-89
4	H	*p*-$NO_2C_6H_4$	40	**4d**	11	125
5	H	$PhCH_2$	40	-	0 (88)[b]	-
6[d]	H	$PhCH_2$	80	**4e**	87	28
7[d]	H	Me	80	**4f**	81	b.p.78-82/3mmHg
8	3-Me	Ph	70	**4g**	58 (75)[c]	92

[a] Reaction time; 3h. [b] Yield of $PhCH_2NHCOO(CH_2)_3I$. [c] Yield of $PhNHCOO$-$CH_2CH(CH_3)CH_2I$ at 40°C. [d] Carried out under the pressure of N_2 (5kg/cm^2).

Table 2. The reactions of unsubstituted oxetane with aromatic isocyanates proceeded more readily than those of alkyl isocyanates or 3-methyloxetane. Even in the latter cases, the yields can be increased to 58-87% by performing these reactions at 70-80°C. One exception was noted, the isocyanate trimer was produced in the reaction of *p*-nitrophenyl isocyanate.

In the case of using benzyl isocyanate or 3-methyloxetane at 40°C, the corresponding 3-iodopropyl carbamates were produced instead of oxazinones in 88% and 75% yields, respectively. These compounds are considered to be hydrolysis products of intermediates II (Scheme 1). Because a similar carbamate was also detected irrespective of the kind of bases (Ph_3P, $Ph_3P=O$) in the reactions of oxetane with phenyl isocyanate even at room temperature as shown in Table 1, the rate determining step is thought to be an intramolecular cyclization of **II**. The Sn-N bond in **II** may be strongly activated by coordination of bases.

Although facile cleavages of cyclic ethers by Me_3SiI have been extensively investigated,[8] a similar cleavage by organotin iodide is scarcely reported. Therefore, in order to elucidate the role of **3** in the oxetane-ring cleavage, following examinations were carried out. 3-Iodopropyl acetate was obtained quantitatively by addition of acetyl chloride to the adduct of oxetane and the complex **3**.[9] On the other hand, the reactions using Bu_2SnI_2 alone and using the complex of Bu_3SnI and $Ph_3P=O$ gave 3-iodopropyl acetate in 25% and 9% yields, respectively.

On the basis of the above results, this cycloaddition reaction can be understood as shown in Scheme 1. The coordination of $Ph_3P=O$ may exert an activation in all steps, especially both the first and last steps, because it has been confirmed that a facile isocyanate-insertion to Sn-O bond occurs even in the absence of bases.[10]

If the tin iodide-base complex could be regenerated in the final step, only a catalytic amount of it would be quite enough. In order to achieve the catalytic cycle illustrated in Scheme 1, the reaction of oxetane and phenyl isocyanate was carried out at 80°C in the presence of 0.1 equivalent of **3**, giving oxazinone **4a** in 60% yield. Apparently this complex can act as a catalyst. Only less than five per cent of oxazinone, however, was produced under milder conditions. We are now investigating an improvement in the catalytic activity, promoting the catalytic reaction at a lower temperature.

Acknowledgement: This work was supported by a Grant-in-Aid (No 60430022) for Scientific Research from the Ministry of Education, Science, and Culture.

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(Received in Japan 23 July 1985)