Cycloaddition of Oxetanes with Heterocumulenes Catalyzed by Organotin Iodide-Lewis Base Complex

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A series of 2-oxazinones **1-8** were synthesized from the cycloaddition reactions of oxetanes with isocyanates by utilizing the complex of diphenyltin diiodide with hexamethylphosphoric triamide (HMPA) as a catalyst. Moreover, the reactions with carbodiimides proceeded under milder conditions with the same catalyst system, and gave 2-iminooxazines, **9** and **10**, in high yields.

In connection with our interest in heterocumulenes chemistry, especially the cycloaddition of them, we have reported that organotin halide-Lewis base complexes played as efficient catalysts for the cycloaddition with oxiranes [1].

On the other hand, cycloadditions of oxetanes with heterocumulenes can be considered as a useful method for preparation of six-membered heterocycles. However, few examples are reported on this type of cycloaddition because of the lower reactivity of oxetanes for ring opening in comparison with oxiranes. As far as we know, only one patent reported the reaction of oxetane with carbodiimides in the presence of triethylamine [2]. Recently, we have described the synthesis of 2-oxazinones from oxetanes and isocyanates in the presence of equimolar amounts of the complex of di-*n*-butyltin diiodide with triphenylphosphine oxide [3]. This is the first example of the cycloaddition of oxetanes with isocyanates. However, when a catalytic amount of this tin complex was used,

Scheme 1
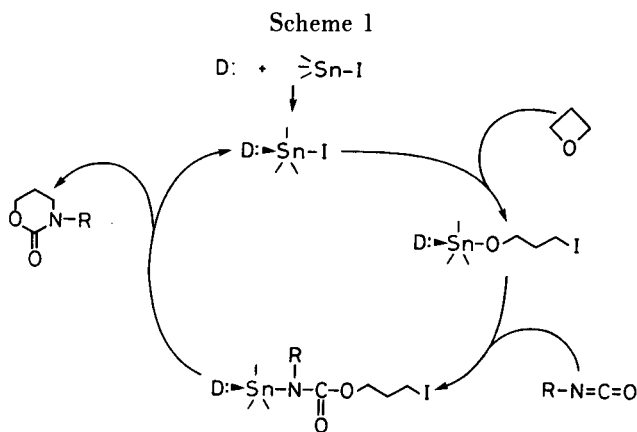
desired 2-oxazinones were scarcely obtained. This might be due to the trimerization of isocyanates, which is generally caused by Lewis bases [4]. Accordingly, it is necessary to develop more effective tin complexes for completing this catalytic reaction without trimerization of iso-
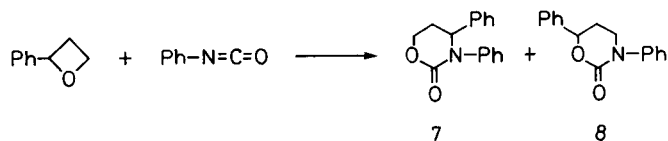
Table 1

2-Oxazinones **1-6**
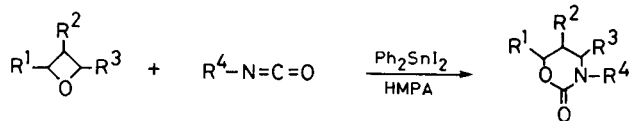
Compound No.	R¹	R²	R³	R⁴	Reaction time (hours)	Yield (%)	Mp or Bp (°C)	Molecular formula	Analyses (%) Calcd./(Found) C	H	N
1	H	H	H	Ph	1	77	97-99	$C_{10}H_{11}NO_2$	67.76 (67.56)	6.26 (6.27)	7.91 (7.93)
2	H	H	H	*p*-Tolyl	1	100	127	$C_{11}H_{13}NO_2$	69.09 (69.05)	6.85 (6.90)	7.22 (7.22)
3	H	H	H	*p*-ClC₆H₄	3	46	88-89	$C_{10}H_{10}ClNO_2$	56.75 (56.77)	4.76 (4.80)	6.62 (6.49)
4	H	H	H	Bu	3	63	81-82/ 0.01 mm Hg	$C_8H_{15}NO_2$	–	–	–
5	H	Me	H	Ph	3	68	92	$C_{11}H_{13}NO_2$	69.06 (69.07)	6.85 (6.79)	7.32 (7.19)
6	Me	H	H	Ph	3	100	78-79	$C_{11}H_{13}NO_2$	69.09 (68.97)	6.85 (6.70)	7.32 (7.45)

cyanates.

Fortunately, we could find that the catalytic activity was increased by the selection of the combination between organotin iodides and Lewis bases. Among the catalysts examined in the reaction of oxetane with phenyl isocyanate, the most effective catalyst was the complex of diphenyltin diiodide with hexamethylphosphoric triamide (HMPA), which afforded 77% yield of 2-oxazinones 1 at 80° for 1 hour. As shown in Scheme 1, similar catalytic cycle which has already proposed in the reaction of oxiranes with heterocumulenes [1] may be also applied in the case of oxetanes, involving the formation of an organotin γ-iodoalkoxide followed by the insertion of an isocyanate [5]. However, the ring cleavage of oxetane and the regeneration of catalyst are considerable problems because the reactivity of oxetanes is lower than that of oxiranes. The choice of the combination of organotin iodide and Lewis base, therefore, is more significant in comparison with the reaction of oxiranes.

Table 1 shows the yields of various 2-oxazinones 1-6 prepared from the cycloaddition of oxetanes with isocyanates carried out at 80°, catalyzed by diphenyltin diiodide-HMPA complex. As to isocyanates, the one bearing an electron donating substituent, p-tolyl isocyanate, showed the highest reactivity, and yielded 2 quantitatively. The reaction of substituted oxetanes includes a problem of the regioselectivity in the ring cleavage. In the reaction of 2-methyloxirane, the cleavage occurred regioselectively to form 6-methyl-2-oxazinone 6 as a sole product. This may be because of the ability of the tin complex to promote the cleavage at the unhindered C-O bond, and similar phenomena have been also observed in the ring cleavage of oxiranes [1] [6]. The 2-oxazinone 6 was confirmed by the comparison of pmr spectra with that of the 4-methyl isomer [7]. On the other hand, 2-phenyloxetane gave both of the isomers. Thus 2-oxazinones, 7 and 8, were obtained in 25% and 41% yields, respectively, at 80° for 3 hours. In

this case, the cleavage of the oxetane at hindered site was accompanied because of the stabilization of a positive charge by conjugative electron release from the π-orbital of an aromatic substituent [8].

Next, we tried the cycloaddition of oxetane with carbodiimides. The reactivity of carbodiimides was higher than that of isocyanates, and the reactions were clean and gave excellent yields. Thus, as shown in Table 2, 2-iminooxazine derivatives, 9 and 10, were obtained almost quantitatively even at 40° for 1 hour.

In conclusion, the catalytic cycloaddition of oxetanes with isocyanates or carbodiimides was achieved by using diphenyltin diiodide-HMPA complex as a catalyst, and offers a convenient and useful method for the preparation of six-membered heterocycles.
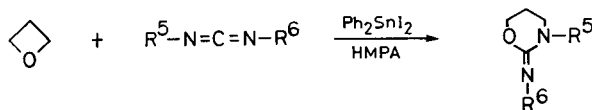
EXPERIMENTAL

Melting points were determined on a Yanaco Micromelting point apparatus and are uncorrected. The ir spectra were measured with a Hitachi 260-3 instrument for potassium bromide discs. The pmr spectra were obtained with a Hitachi R-90HS instrument operating at 90 MHz. Mass spectra were reported on a Hitachi RMU-6E instrument. Analytical GLC were performed on a Shimazu GC-3B with TCD using a 2 m x 3 mm glass column packed with Silicone OV-17 on Uniport HP (5% 60-80 mesh), helium as a carrier gas.

General Procedure for Preparation of 2-Oxazinones 1-6.

The reactions were performed in a sealed tube. To a solution of diphenyltin diiodide (0.52 g, 1 mmole) and HMPA (0.18 g, 1 mmole) in oxetane (15 mmoles) was added an isocyanate (10 mmoles) with stirring under dry nitrogen. The tube was sealed and heated at 80° for the time indicated in Table 1. After the reaction, the resulting mixture was chromatographed on silica gel with chloroform as eluent. The yields of products were determined by glc based on isocyanates used and are shown with spectral data in Tables 1 and 3.

Table 2

2-Iminooxazines 9, 10

Compound No.	R^5	R^6	Yield (%)	Mp or Bp (°C)	Molecular formula	Analyses (%) Calcd./(Found)		
						C	H	N
9	Ph	Ph	93	106-107	$C_{16}H_{16}N_2O$	76.16 (76.02)	6.39 (6.38)	11.10 (11.16)
10	Bu	Bu	91	65/0.1 mm Hg	$C_{12}H_{24}N_2O$	67.44 (67.88)	11.43 (11.39)	13.01 (13.19)

Table 3

Spectra of 2-Oxazinones **1-6**

Compound No.	IR ν cm^{-1} (C=O)	Mass Spectrum m/e	PMR (deuteriochloroform/TMS) δ (ppm)
1	1680	177 (M$^+$)	2.10-2.40 (m, 2H, CH$_2$), 3.70 (t, 2H, NCH$_2$), 4.40 (t, 2H, OCH$_2$), 7.20-7.60 (m, 5H, aromatic)
2	1685	191 (M$^+$)	2.00-2.40 (m, 2H, CH$_2$), 2.35 (s, 3H, CH$_3$), 3.70 (t, 3H, NCH$_2$), 4.40 (t, 3H, OCH$_2$), 7.10-7.50 (m, 4H, aromatic)
3	1670	211 (M$^+$)	2.10-2.40 (m, 2H, CH$_2$), 3.70 (t, 2H, NCH$_2$), 4.45 (t, 2H, OCH$_2$), 7.20-7.40 (m, 4H, aromatic)
4	1680	157 (M$^+$)	0.80-1.90 (m, 7H, NCC$_3$H$_7$), 1.90-2.30 (m, 2H, CH$_2$ of oxazine ring), 3.20-3.60 (m, 4H, 2 NCH$_2$), 4.25 (t, 2H, OCH$_2$)
5	1680	191 (M$^+$)	1.10 (d, 3H, CH$_3$), 2.20-2.60 (m, 1H, CH), 3.20-3.90 (m, 2H, NCH$_2$), 3.90-4.50 (m, 2H, OCH$_2$), 7.20-7.60 (m, 5H, aromatic)
6	1685	191 (M$^+$)	1.50 (d, 3H, CH$_3$), 2.00-2.30 (m, 2H, CH$_2$), 3.50-3.90 (m, 2H, NCH$_2$), 4.40-4.80 (m, 1H, OCH), 7.20-7.80 (m, 5H, aromatic)

Table 4

Spectra of 2-Iminooxazines **9, 10**

Compound No.	IR ν cm^{-1} (C=N)	Mass Spectrum m/e	PMR (deuteriochloroform/TMS) δ (ppm)
9	1640	252 (M$^+$)	2.00-2.40 (m, 2H, CH$_2$), 3.70 (t, 2H, NCH$_2$), 4.30 (t, 2H, OCH$_2$), 6.80-7.70 (m, 10H, aromatic)
10	1660	212 (M$^+$)	0.80-1.80 (m, 14H, 2 NCC$_3$H$_7$), 1.80-2.20 (m, 2H, CH$_2$), 3.00-3.50 (m, 6H, 3 NCH$_2$), 4.10 (t, 2H, OCH$_2$)

Compounds **7** and **8** were separated by column chromatography, and the spectral data are as follows.

3,4-Diphenyl-1,3-oxazin-2-one (7).

This compound was obtained in 25% yield, mp 143-144°; ir (potassium bromide): 1680 cm^{-1} (C=O); pmr (deuteriochloroform/TMS): δ 2.00-2.80 (m, 2H), 4.30-4.50 (m, 2H), 5.00-5.20 (m, 1H), 7.20-7.60 (m, 10H); ms: m/e 253 (M$^+$).

Anal. Calcd. for C$_{16}$H$_{15}$NO$_2$: C, 75.87; H, 5.97; N, 5.53. Found: C, 75.64; H, 5.86; N, 5.83.

3,6-Diphenyl-1,3-oxazin-2-one (8).

This compound was obtained in 41% yield, mp 196-197°; ir (potassium bromide): 1680 cm^{-1} (C=O); pmr (deuteriochloroform/TMS): δ 2.00-2.50 (m, 2H), 3.50-4.00 (M, 2H), 5.40-5.60 (m, 1H), 7.00-7.60 (m, 10H); ms: m/e 253 (M$^+$).

Anal. Calcd. for C$_{16}$H$_{15}$NO$_2$: C, 75.87; H, 5.97; N, 5.53. Found: C, 75.68; H, 5.88; N, 5.51.

2-(Phenylimino)-3-phenyl-1,3-oxazine (9) and **2-(Butylimino)-3-butyl-1,3-oxazine (10).**

To a solution of diphenyltin diiodide (0.52 g, 1 mmole) and HMPA (0.18 g, 1 mmole) in oxetane (15 mmoles) was added a carbodiimide (10 mmoles). The mixture was stirred for an hour at 40° in a 30 ml round bottomed flask under dry nitrogen. The compound **9** was isolated as precipitates by adding a large amount of hexane to the reaction mixture, and purified by recrystallization from benzene-hexane. Compound **10** was isolated by column chromatography, and purified by distillation. The

yields were determined by glc based on carbodiimides used, and are shown with spectral data in Tables 2 and 4.

REFERENCES AND NOTES

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[5] We have reported the reaction of Bu$_3$SnO(CH$_2$)$_3$X with heterocumulenes, and these features were consistent with the direct cycloaddition of oxetanes with heterocumulenes such that the cycloaddition may proceed *via* an organotin γ-haloalkoxide. A. Baba, H. Kishiki, I. Shibata and H. Matsuda, *Organometallics*, **4**, 1329 (1985).

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[7] 4-Methyl-3-phenyl-2-oxazinone was prepared by our previous method [5] using tributyltin γ-iodoalkoxide (Bu$_3$SnOCH$_2$CH$_2$CHMeI) and phenyl isocyanate. The spectral and physical data are as follows: mp 116°; ir (potassium bromide): 1690 cm^{-1} (C=O); pmr: δ 1.15 (d, 3H, CH$_3$), 1.70-2.60 (m, 2H, CH$_2$), 3.80-4.30 (m, 1H, NCH), 4.30-4.60 (m, 2H, OCH$_2$), 7.10-7.70 (m, 5H, aromatic); ms: m/e 191 (M$^+$).
Anal. Calcd. for C$_{11}$H$_{13}$NO$_2$: C, 69.09; H, 6.85; N, 7.32. Found: C, 68.83; H, 6.81; N, 7.26.

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