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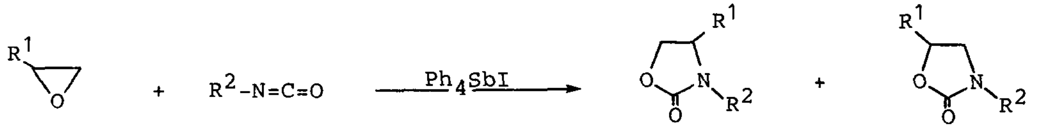
UNUSUAL CYCLOADDITION OF OXIRANES WITH ISOCYANATES CATALYZED BY TETRAPHENYLSTIBONIUM IODIDE; SELECTIVE FORMATION OF 3,4-DISUBSTITUTED OXAZOLIDINONES.

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

Abstract Tetraphenylstibonium iodide is a general and versatile catalyst for the selective formation of unusual cycloadducts, 3,4-disubstituted oxazolidinones, in the reaction of oxiranes with isocyanates.

The cycloaddition of oxiranes with isocyanates is well confirmed method for preparing a variety of 2-oxazolidinones, and many kinds of catalyst have been known.[1] However, 3,5-disubstituted 2-oxazolidinones **5** have been exclusively produced in almost all reactions of monosubstituted oxiranes with isocyanates. No catalyst which gives predominantly 3,4-disubstituted 2-oxazolidinones **4** has been developed so far. Although Braun et al. attempted the synthesis of 3-phenyl-4-methyl-2-oxazolidinone (**4a**) by using strong acid $AlCl_3$ as catalyst at 160°C, 3,5-disubstituted oxazolidinone **5a** is exclusively obtained , while 3,4-diphenyl-2-oxazolidinone can be obtained in 24% yield among with 46% of 3,5-diphenyl-2-oxazolidinone.[2,3]

Here, we wish to describe the first and general selective formation of **4** by the cycloaddition of oxiranes with isocyanates. Tetraphenylstibonium iodide (**3**) is found to be a versatile catalyst for selective formations of **4** under mild conditions.



1 **2** **3** **4a-e** **5a-e**

a; R^1 = Me R^2 = Ph
b; Et Ph
c; Ph n-Bu
d; R^1 = Et R^2 = n-Bu
e; Ph Ph
f; di-Me Ph

The reaction of 2-ethyloxirane (**1b**) with phenyl isocyanate (**2a**) is described as a typical procedure. To a solution of **1b** (30 mmol) and **3** (1 mmol) in 5 ml of CH_2Cl_2 was added very slowly 10 mmol of **2a** for 60 min at 45°C. After heating for 1 h, volatile compoumds were removed under reduced pressure, then the resulted mixture was subjected to silica gel column chromatography, yielding nearly pure **4b** (eluted by $CHCl_3$).[4]

Reaction conditions and results are summarized in Table 1. A choice of solvent is significant as exemplified in the reactions of 2-methyloxirane with phenyl isocyanate. Although CH_2Cl_2 is the most suitable solvent in the reaction with 2-methyloxirane, a preferable solvent is benzene in other cases. Because good or exellent selective formations of **4** were achieved in several combinations between typical oxiranes and isocyanates, organoantimony iodide **3** can be considerd as a widely effective catalyst for this unusual cycloaddition.

Since to our knowledge no cycloaddition with isocyanates via α-cleavage of oxiranes except 2-phenyloxirane has been reported, it is most noteworthy

Table 1. Formations of 3,4-Disubstituted Oxazolidinones.[a]

Entry	R^1	R^2	Solvent	Yield (%)[h]	Ratio[h]
				(**4** + **5**)	**4** : **5**
1[b]	Me	Ph	—	100	52 : 48
2[b,c]			—	73	25 : 75
3			Benzene	100	59 : 41
4			HMPA	100	66 : 34
5			THF	100	50 : 50
6			CH_2Cl_2	100	80 : 20
7			CH_3CN	85	78 : 22
8	Et	Ph	Benzene	86	78 : 22
9			CH_2Cl_2	84	100 : 0
10	Ph	n-Bu	Benzene	69	92 : 8
11[d]			CH_2Cl_2	59	89 : 11
12[e]			CH_3CN	68	82 : 18
13	Et	n-Bu	Benzene	100	93 : 7
14[f]			CH_3CN	46	100 : 0
15	Ph	Ph	Benzene	86	99 : 1
16			CH_3CN	54	97 : 3
17[g]	2,2-di-Me	Ph	Benzene	0	-

[a] Oxirane/isocyanate/Ph_4SbI = 30/10/1 mmol, 45°C, 1 h, solvent 5 ml. Isocyanate was dropwised for 60 min. [b] Oxirane 100 mmol, 36°C. [c] Isocyanate was added at once. Trimer was isolated (27%). [d] 45°C, 3 h. [e] 45°C, 4 h. [f] 45°C, 5 h. [g] 60°C, 1 h, triphenyl isocyanurate was yielded quantitatively. [h] Determined by GLC.

Table 2. Cycloadditions Using Catalysts Except Ph_4SbI^a

Entry	R^1	R^2	Cat.	Yield (%) (**4** + **5**)	Ratio **4** : **5**
1	Ph	Ph	Ph_4SbBr	78	97 : 3
2			Ph_4SbOAc	0	
3			Ph_3Sb	0	
4			Bu_4NI	0	
5			Ph_4PI	0	
6			LiBr-HMPA[b]	100	13 : 87
7	Et	n-Bu	Ph_4SbBr	12	23 : 77

[a] Solv. Benzene 5 ml, 45°C, 1 h, other conditions are similar to those in Table 1. [b] LiBr/HMPA = 1/2 mmol.

that the 3,4-disubstituted adducts **4** were selectively obtained even in the reactions using 2-alkyloxiranes.[3] Moreover, the catalyst **3** could allow this addition under very mild conditions in comparison with a conventional catalyst, Bu_4NI, which could not promote the addition of 2-phenyloxirane with phenyl isocyanate under similar conditions. Apparently, the catalyst **3** not only gives **4** selectively, but also activates this cycloaddition greatly. As shown in Table 2, tetraphenylstibonium bromide could also promote only the formation of **4e**, but Ph_4SbOAc bearing no halogen was not effective at all, yielding triphenyl isocyanurate by trimerization of phenyl isocyanate. On the other hand, little consumption of isocyanate was caused by Ph_3Sb or Ph_4PI. Even the complex LiBr-HMPA[6] which is reported to be one of the most effective catalysts gave 3,5-disubstituted oxazolidinone **5e** predominantly (Entry 6 in Table 2).

In the reaction with 2,2-dimethyloxirane, the formation of **4f** was hardly thought to occur because of the hindered configuration between 3-phenyl and 4-methly groups, therefore, the formation of **5f** was expected in this case. However, neither **4f** nor **5f** was obtained, and triphenyl isocyanurate was yielded quantitatively. From this result, it is suggested that a β-cleavage of oxirane would been hardly promoted by Ph_4SbI in contrast with a facile α-cleavage in cycloaddition of oxiranes with isocyanates, though the details have not been clear as yet.

Weiner demonstrated that an isocyanate is readily trimerized at first and resulting trimer reacts with an oxirane, yielding an oxazolidinone.[6] Because sometimes the formation of isocyanate trimers was observed in our case,[7] the reaction of trimers and oxiranes may be also considered. However, triphenyl isocyanurate did not react with 2-phenyloxirane at all in the presence of 3 even at 70°C for 20 h.

Next, the possibility of interconversion of **4** and **5** could be excluded in the following way. A solution of **4a** (5 mmol) and **3** (0.5 mmol) in benzene (5 ml) was heated at 45°C for 1 h. The compound **4a**, however, was recovered quantitatively, and neither **5a** nor triphenyl isocyanurate was detected at all. In a similar manner, no change of **5a** was observed.

For the selective formation of **4**, slow dropwise addition of isocyanates is very important. When **2a** was added at once, the exothermal trimerization of phenyl isocyanate was accompanied by the formation of **5a** and **4a.** It is interesting that the yield of **5a** is little affected (48-54%) in spite of the significant decrease of the yield of **4a** (52-19%), and the trimer was obtained in 27% yield (Entry 1, 2 in Table 1). The formation of trimer may be closely related to that of **4**, since the amount of former nearly consists with the decrement of latter.

These results suggest that the formation course of **4** may be independent of the formation of **5**. Now we are investigating the detail reaction path of unusual cycloaddition.

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3. A few of **4** are already obtained only in the reaction using 2-phenyloxirane, but the selectivities are lower than 35% in all cases. Ref. 2; W. J. Irwin, D. L. Wheeler, J. Chem. Soc. (C), **1971**, 3166; J. E. Herweh, J. Org. Chem., **33**, 4029 (1968).
4. The structure of **4a** was determined in comparison with the spectral data of **5a** as follows. **4a**; mp 51°C; MS 177 (M+), 162, 118, 104; IR (neat) 1740 cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.25 (d, J = 3.0 Hz, 3H), 3.9-4.17 (m, 1H), 4.35-4.7 (m, 2H), 7.08-7.55 (m, 5H). **5a**: mp 81°C; MS 177 (M+), 132, 104; IR (KBr) 1740 cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.52 (d, J = 3.0 Hz, 3H), 3.6 (t, J = 3.7 Hz, 1H), 4.1 (t, J = 4.2 Hz, 1H), 4.61-4.92 (m, 1H), 7.0-7.6 (m, 5H). The other products were also characterized by MS and ^1H NMR spectra. Bps (or mp) of these adducts are as follows; **4b**; 125°C/2 mmHg **4c**; 129°C/0.01 mmHg **4d**; 107°C/2 mmHg **4e**; mp 130°C.
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6. M. L. Weiner, J. Org. Chem., **26**, 951 (1961). In this report no 3,4-disubstituted oxazolidinone has been detected.
7. The trimerization was caused by the combination of 3 and oxirane, and no consumption of isocyanate was observed in the presence of either of them.

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