SELECTIVE SYNTHESIS OF FIVE AND SIX MEMBERED CYCLIC CARBAMATES BY THE REACTION OF 2-(1-HALOALKYL)OXIRANES WITH CARBON DIOXIDE AND ALIPHATIC PRIMARY AMINES†

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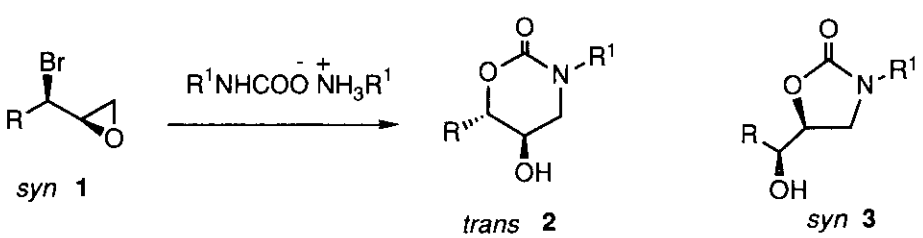
Abstract - The reaction of 2-(1-haloalkyl)oxiranes with carbamate salts selectively gave perhydrooxazin-2-ones at neutral conditions and oxazolidin-2-ones at basic. Those reactions proceeded stereospecifically and the mechanisms were discussed.

Among many kinds of carbon dioxide (CO_2) fixation reactions,[1-4] the most facile method is the reaction of amines and CO_2 to give carbamate salts. The carbamate salts have been attempted to assemble to organic compounds,[2] but the examples to build up heterocycles are rarely known.[3] We have reported the reaction of epichlorohydrin with carbamate salts to afford perhydrooxazinones in low yields (3-36%).[4] In order to improve the yield and to examine the stereochemistry, we have prepared 2-(1-haloalkyl)oxiranes (**1**).[5] The reaction of **1** with carbamate salts gave a new result that under neutral or strong basic conditions, six membered cyclic carbamates, namely perhydrooxazin-2-ones (**2**)[6] or five membered cyclic carbamates, oxazolidin-2-ones (**3**)[6] were obtained, respectively. The reactions of *syn* **1** gave stereospecifically *trans* **2** or *syn* **3** according to the basicity of the reaction medium. Here, we report the selective reaction and discuss the mechanisms.



syn **1** *trans* **2** *syn* **3**

Table 1. The Cyclic Carbamates Prepared from the Oxirane (**1**) with Carbamate salts

	1		Carbamate		Yield / %[a]	
Entry	R	X	Salt, R^1	Method	**2**	**3**
1	Ph	Br	Et	A	25	
2	Ph	Br	Et	B		53
3	Ph	Br	c-C_6H_{11}	A	30	
4	Ph	Br	c-C_6H_{11}	B		53
5	Ph	Br	$PhCH_2$	A	48	
6	Ph	Br	$PhCH_2$	B		49
7	Ph	Br	$PhCH_2$	A[b]		51
8	Ph	Br	$PhCH_2CH_2$	A	77	
9	Ph	Br	$PhCH_2CH_2$	B		59
10	Ph	Cl	$PhCH_2$	A	49	
11	Ph	Cl	$PhCH_2$	B		44
12	Pr	Br[c]	$PhCH_2$	A	34	
13	Pr	Br	$PhCH_2$	B		14
14	Me	Br[d]	$PhCH_2$	A	21	

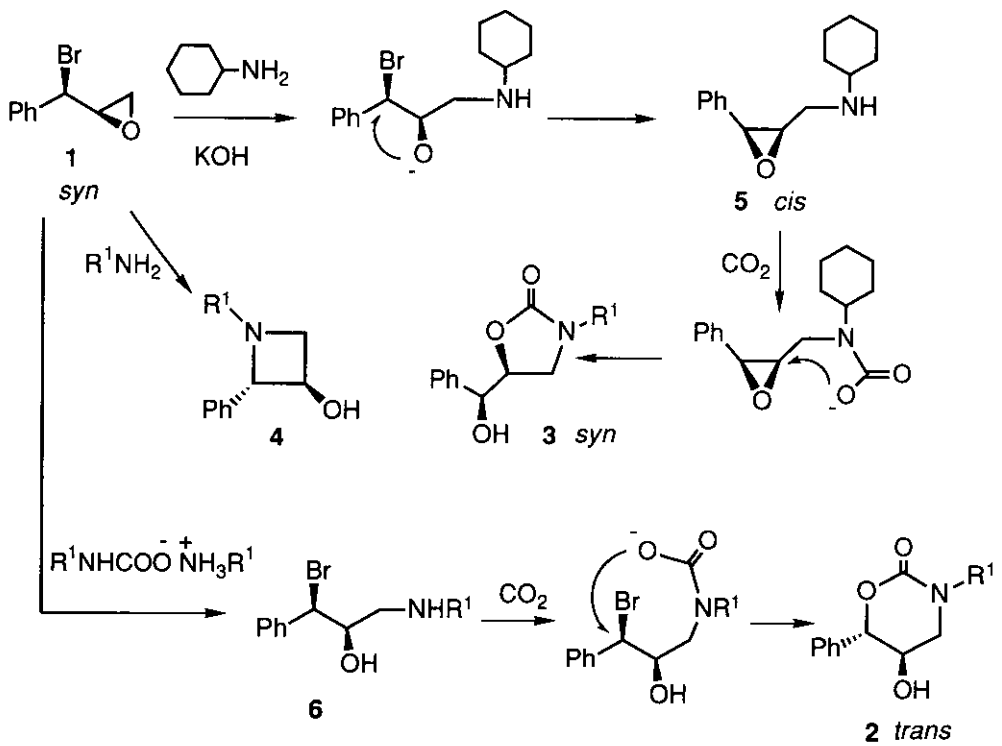
a) Isolated yield. b) KOH was added to the solution of Method A. c) This oxirane was prepared as the same manner as ref. 7. d) Ref. 7.

The experiment was as follows and the results were summarized in Table 1.

Method A: treatment of **1** (10 mmol) with a carbamate amine salt prepared from an aliphatic primary amine (30 mmol) and CO_2 in methanol (10 ml) at room temperature for 24-72 h gave **2**.

Method B: treatment of **1** (10 mmol) with the mixture of an aliphatic primary amine (15 mmol) and Cs_2CO_3 (15 mmol) in methanol (10 ml) at room temperature for 24-72 h gave **3**.

We have already reported the reaction of **1** with aliphatic primary amines to give azetidine derivatives (**4**),[8] which did not undergo further reaction with CO_2. On the other hand, the reaction of *syn* **1** with cyclohexylamine in the presence of KOH gave *cis*-aminomethyloxirane (**5**),[9] which further reacted with CO_2 to afford **3** (yield 45% from **1**). Those stereospecific results show that the amine attacked to the end of the oxirane carbon in alkaline medium to open the oxirane ring and to eliminate bromine anion successively, and the epoxy group migrated to give **5**. Through the reaction, the alkali acts as the promoter for migration of the epoxy group. Indeed, the reaction of an amine with Cs_2CO_3 by Method B gives the carbamate cesium salt and



$$R^1NH_2 + CO_2 \rightleftharpoons R^1NHCOO^- {}^+NH_3R^1 \qquad \text{(eq. 1)}$$

equimolar of strong base CsOH. Therefore, the five membered cyclic carbamates (**3**) were obtained by Method B. Furthermore, even in the reaction carried out by Method A, **3** was also obtained by the addition of KOH to the reaction mixture (run 7).

In the method A, the species first attacks to **1** is not the carbamate anion, but the amine formed under the equilibrium with the carbamate ammonium salt (eq. 1). The amine opens the oxirane ring, and the resulting alkoxide anion is protonated to form the initial intermediate (**6**) on account of neutral or weak basic reaction conditions.[10] Since **6** does not form a new epoxy group, **6** reacts with CO_2 formed under the equilibrium and the carbamate anion attacks to the back of the bromine atom to give **2** stereospecifically.

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†Dedicated to Professor Edward C. Taylor on the occasion of his 70th birthday.

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6. The Physical data or those compounds show typically as follows; **2** (R=Ph, R^1=$PhCH_2$): mp 168-169 °C; ir (KBr) 3260, 1661 cm^{-1}; ^1H nmr (300 MHz, $CDCl_3$) δ 2.78 (1H, br s, OH), 3.15 (1H, dd, *J* = 12.0, 6.0 Hz, CH_2-N), 3.27 (1H, dd, *J* = 12.0, 4.8 Hz, CH_2-N), 4.06 (1H, ddd, *J* = 6.3, 6.0, 4.8 Hz, CH-OH), 4.48 (1H, d, *J* = 14.7 Hz, $PhCH_2$), 4.65 (1H, d, *J* = 14.7 Hz, $PhCH_2$), 5.18 (1H, *J* = 6.3 Hz, PhCH), 7.24-7.37 (10H, m); ^{13}C nmr (75 MHz, $CDCl_3$) δ 48.68 (CH_2-N), 52.67 ($PhCH_2$), 66.09 (CH-OH), 82.20 (PhCH), 125.91, 127.74, 128.04, 126.63, 128.72, 135.95, 136.19, 153.20 (C=O); **3** (R=Ph, R^1=$PhCH_2$): mp 108-109 °C; ir (KBr) 3350, 1743 cm^{-1}; ^1H nmr (300 MHz, $CDCl_3$) δ 2.81(1H, d, *J* = 3.0 Hz, OH), 3.15 (1H, dd, *J* = 9.0, 6.0 Hz, CH_2-N), 3.23 (1H, dd, *J* = 9.0, 8.4 Hz, CH_2-N), 4.33 (1H, d, *J* = 15.0 Hz, $PhCH_2$), 4.38 (1H, d, *J* = 15.0 Hz, $PhCH_2$), 4.63 (1H, ddd, *J* = 8.4, 6.6, 6.0 Hz, CH-O), 4.68 (1H, dd, *J* = 6.6, 3.0 Hz, CH-OH), 7.14-7.19 (2H, m), 7.23-7.38 (8H, m); ^{13}C nmr (75 MHz, $CDCl_3$), δ 45.17 (CH_2-N), 48.11 ($PhCH_2$), 75.22 (CH-OH), 76.16 (CH-O), 126.93, 127.87 128.69, 128.73, 135.27, 137.31, 157.29 (C=O).
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9. The aminomethyloxirane was confirmed with spectra: ir (neat) 3280, 1112 cm^{-1}; ^1H nmr (300 MHz, $CDCl_3$) δ 0.90-1.29 (5H, m, cyclohexyl), 1.54-1.78 (5H, m, cyclohexyl), 2.32-2.41 (1H, m, NH-CH), 2.56 (1H, brs, NH), 2.58 (1H, dd, *J* = 13.2, 6.6 Hz, CH_2-NH), 2.64 (1H, dd, *J* = 13.2, 5.2 Hz, CH_2-NH), 3.42 (1H, ddd, *J* = 6.6, 5.2, 4.5 Hz, O-CH), 4.13 (1H, d, *J* = 4.5 Hz, PhCH), 7.26-7.39 (5H, m); ^{13}C nmr (75 MHz, $CDCl_3$) δ 24.74, 24.78, 32.89, 43.70 (CH_2), 56.28 (NHCH), 56.92 (J_{CH} = 172.8 Hz, PhCH), 57.99 (J_{CH} = 174.9 Hz, O-CH), 126.13, 127.65, 128.08, 134.93.
10. The reaction mixture is initially basic and gradually neutral according to HBr formation.

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