The Formation of Cyclic Ethers from Diallyldibutyltin and Halo Ketones Catalyzed by Tetraethylammonium Chloride

Katsunori Yano, Yukio Hatta, Akio Baba,* Haruo Matsuda
Department of Applied Chemistry, Faculty of Engineering, Osaka University, 2-1 Yamadaoka, Suita, Osaka 565, Japan

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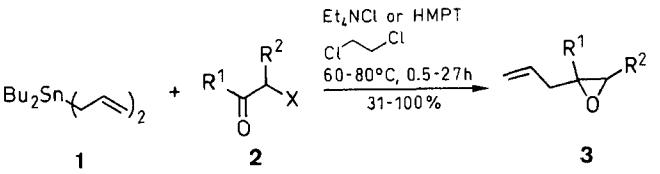
The cyclization reaction of diallyldibutyltin and α- or γ-halo ketones, especially chloro-substituted ketones, effectively proceeds in the presence of a catalytic amount of tetraethylammonium chloride, producing the corresponding 2-allyloxiranes or 2-allyltetrahydrofurans in high yield, respectively. β-Chloro ketones give the corresponding allyl alcohols.

The palladium-catalyzed reaction of α-halo ketones with allyl-substituted tin compounds such as allyltributyltin or diallyldibutyltin is a useful route to allyloxiranes.[1,2] In this method, however, there has been a significant limitation; aromatic chloro ketones are unadaptable because of their low reactivity and the facile rearrangement of the resultant oxiranes to the corresponding aldehydes. The acidity of the palladium catalysts seems likely to be responsible for this rearrangement under the reaction conditions, so an alternative catalytic system was required to overcome the limitation. Quite recently, we have proposed a catalyst, dibutyltin dichloride–hexamethylphsophoric triamide (HMPT) system, for the allyloxirane formation from allyltributyltin and α-halo ketones in the presence of a radical inhibitor, where allyldibutyltin chloride is assumed to act as an active species.[3] In this paper we wish to report a more effective allylation which was achieved by using diallyldibutyltin (**1**) with a catalytic amount of tetraethylammonium chloride (Et_4NCl), furnishing 2-allyloxiranes **3a–g** and 2-allyltetrahydrofurans **8j,k** from α- and γ-halo ketones, respectively.



Substrate	R^1	R^2	X	Substrate	R^1	R^2	X
2aa	Ph	H	Cl	**2db**	Ph	Me	Br
2ab	Ph	H	Br	**2ea**	Ph	Ph	Cl
2ba	4-ClC_6H_4	H	Cl	**2eb**	Ph	Ph	Br
2bb	4-ClC_6H_4	H	Br	**2fb**	Et	H	Br
2cb	4-$O_2NC_6H_4$	H	Br	**2gb**	*t*-Bu	H	Br
2da	Ph	Me	Cl				

Scheme 1

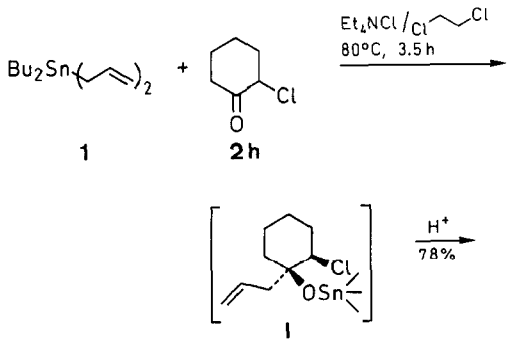
The results summarized in Table 1 demonstrate the facile formation of allyloxiranes from **1** and α-chloro ketones. No rearrangement of the resultant oxiranes produced was detected in all runs, presumably due to the neutrality of our reaction conditions, where no Lewis acid catalyst was used. Moreover, no radical quencher was required except for secondary halo ketones. Et_4NCl was more effective than HMPT, while the latter was the most effective one in the allylation with allyltributyltin (entries 1 and 2).[3] Without the additive, the starting chloro ketone **2aa** was

Table 1. Allylation–Cyclization of α-Halo Ketones by Diallyldibutyltin (**1**)

Entry	Substrate	Additive	Temp. (°C)	Time (h)	Product	Yield (%)[a]	bp (°C)/Torr	Molecular Formula
1	**2aa**	Et_4NCl	60	1	**3a**	76	60/3	$C_{11}H_{12}O$[b] (160.2)
2	**2aa**	HMPT	60	20	**3a**	trace		
3	**2aa**	–	60	20	**3a**	trace		
4	**2ab**	Et_4NCl	60	1	**3a**	100		
5	**2ab**	HMPT	60	2	**3a**	86		
6	**2ba**	Et_4NCl	60	1	**3b**	31	65/3	$C_{11}H_{11}ClO$[b] (194.7)
7	**2bb**	Et_4NCl	60	0.5	**3b**	57		
8	**2cb**	HMPT	60	0.7	**3c**	88	100/3	$C_{11}H_{11}NO_3$[c] (205.2)
9	**2da**	Et_4NCl	80	7.5	**3d**	75(4)[d] (68/32)[e]	(*cis*) 90/10	$C_{12}H_{14}O$[b] (174.2)
10[f]	**2da**	Et_4NCl	80	6	**3d**	80 (57/43)[e]	(*trans*) 100/10	$C_{12}H_{14}O$[b] (174.2)
11	**2db**	Et_4NCl	80	5.5	**3d**	46(19)[d] (51/49)[e]		
12[f]	**2db**	Et_4NCl	80	7	**3d**	97 (55/45)[e]		
13[f]	**2ea**	Et_4NCl	80	4.5	**3e**	52 (60/40)[e]	(*cis*) 103/4	$C_{17}H_{16}O$[b] (236.3)
14[f]	**2eb**	Et_4NCl	80	6	**3e**	40 (52/48)[e]	(*trans*) 120/4	$C_{17}H_{16}O$[b] (236.3)
15	**2fb**	Et_4NCl	60	3.5	**3f**	43	65/150	$C_7H_{12}O$[c] (112.2)
16	**2gb**	Et_4NCl	60	27	**3g**	83	50/100	$C_9H_{16}O$[b] (140.2)

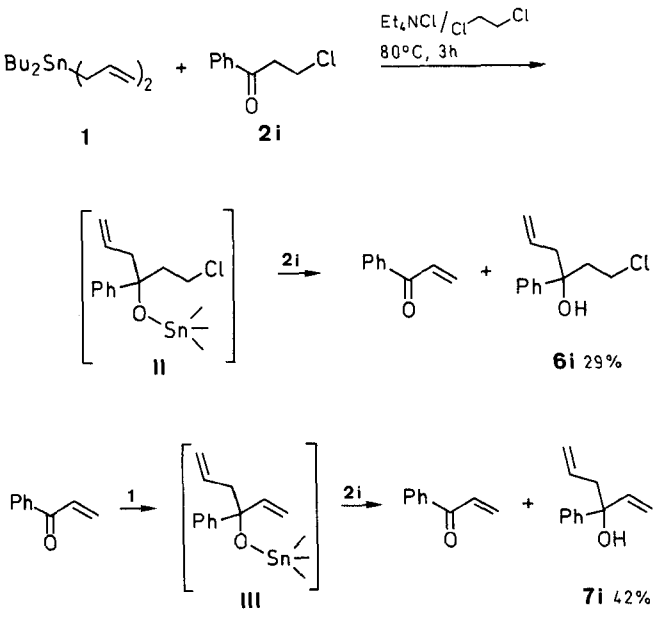
[a] Yield determined by GLC.
[b] Satisfactory HRMS obtained: $m/z \pm 0.0015$.
[c] Satisfactory microanalyses obtained: C ± 0.25, H ± 0.22.
[d] Yield of byproduct **4d** in brackets.
[e] Ratio of *cis*/*trans*.
[f] DNB (0.2 mmol).

hardly consumed even after 20 hours (entry 3). Although the role of Et_4NCl has not been revealed, the elimination of the tin halides is plausibly enhanced as already reported in the formation of carbonates[4] and allyl ketones.[5] The reaction with α-bromo ketones took place more readily (entries 4 and 7), and was effected even by HMPT (entries 5 and 8). Noteworthy is the fact that a hindered bromo ketone **2gb** was adaptable (entry 16), while our reported method using allyltributyltin failed in the synthesis of it.[3] In the case of secondary halo ketones which are particularly apt to react in a radical manner, the addition of *p*-dinitrobenzene (DNB) was required to inhibit the radical coupling affording, e.g., 2-methyl-1-phenyl-4-penten-1-one **(4d)** (entries 9–14).



Scheme 2

On the other hand, the allylation of 2-chlorocyclohexan-1-one **(2h)** gave only the corresponding *cis*-1-allyl-2-chlorocyclohexanol **(5h)** in 78% yield (Scheme 2). This result indicates the idea that the attack of **1** predominantly occurred at the less hindered site of the carbonyl group.[6] The formation of the cis isomer **I** could



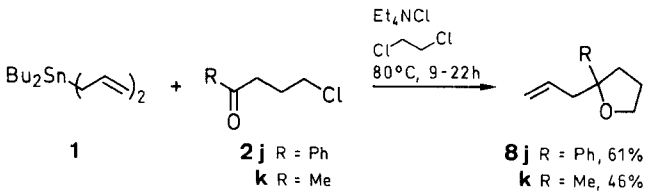
Scheme 3

Table 2. 2-Allyloxiranes **3a–g** and 2-Allyltetrahydrofurans **8j,k** Prepared

Product	^{1}H NMR ($CDCl_3$/TMS) δ, J (Hz)	^{13}C NMR ($CDCl_3$) δ	MS m/z (%)
3a	2.68–2.87 (m, 3H, allylic CH_2 and one of ring CH_2), 3.00 (d, 1H, J = 5.9), 5.08 (d, 1H, J = 11.3), 5.11 (d, 1H, J = 16.3), 5.58–6.03 (m, 1H), 7.35 (s, 5H)	39.18 (t), 54.30 (t), 58.85 (s), 117.93 (t), 125.53 (d), 127.05 (d), 127.87 (d), 132.42 (d), 139.73 (s)	160 (M^+, 6), 131 (100)
3b	2.61 (dd, 1H, J = 7.3, 15.1), 2.72 (d, 1H, J = 5.4), 2.87 (dd, 1H, J = 6.4, 15.1), 3.00 (d, 1H, J = 5.4), 5.10 (d, 1H, J = 10.3), 5.12 (d, 1H, J = 17.1), 5.70–5.80 (m, 1H), 7.31 (s, 4H)	39.18 (t), 54.61 (t), 58.66 (s), 118.42 (t), 127,17 (d), 128.21 (d), 132.17 (d), 133.09 (s), 138.39 (s)	194 (M^+, 7), 165 (100)
3c	2.70–2.94 {m, 3H, allylic CH_2, and one of ring CH_2 (δ = 2.77, d, 1H, J = 5.0)}, 3.10 (d, 1H, J = 5.0), 5.17 (d, 1H, J = 11.9), 5.18 (d, 1H, J = 15.0), 5.50–6.03 (m, 1H), 7.58 (d, 2H, J = 8.8), 8.23 (d, 2H, J = 8.8)	38.75 (t), 54.88 (t), 58.57 (s), 118.91 (t), 123.27 (d), 126.65 (d), 131.59 (d), 147.02 (s), 147.24 (s)	205 (M^+, 4), 204 ($M^+ - 1$, 3), 150 (100)
3d (*cis*)	0.98 (d, 3H, J = 5.4), 2.50 (dd, 1H, J = 7.3, 14.7), 2.83 (dd, 1H, J = 6.4, 14.7), 3.21 (q, 1H, J = 5.4), 5.04 (d, 1H, J = 9.3), 5.05 (d, 1H, J = 18.1), 5.68–5.79 (m, 1H), 7.24–7.36 (m, 5H)	13.81 (q), 41.34 (t), 58.42 (d), 64.21 (s), 117.36 (t), 125.31 (d), 126.35 (d), 127.29 (d), 132.20 (d), 137.75 (s)	174 (M^+, 4), 173 ($M^+ - 1$, 7), 105 (100)
3d (*trans*)	1.47 (d, 3H, J = 5.4), 2.60 (dd, 1H, J = 6.8, 15.1), 2.84 (dd, 1H, J = 6.8, 15.1), 3.01 (q, 1H, J = 5.4), 5.07 (d, 1H, J = 9.3), 5.09 (d, 1H, J = 18.6), 5.68–5.81 (m, 1H), 7.24–7.36 (m, 5H)	13.81 (q), 35.43 (t), 61.16 (d), 62.26 (s), 117.11 (t), 125.31 (d), 126.35 (d), 127.42 (d), 132.63 (d), 140.68 (s)	174 (M^+, 4), 173 ($M^+ - 1$, 7), 105 (100)
3e (*cis*)	2.69 (dd, 1H, J = 7.6, 14.4), 2.88 (dd, 1H, J = 6.6, 14.4), 4.18 (s, 1H), 5.11 (d, 1H, J = 10.3), 5.12 (d, 1H, J = 17.6), 6.99–7.16 (m, 10H)	43.06 (t), 63.67 (d), 68.29 (s), 118.62 (t), 126.51 (d), 127.14 (d), 127.30 (d), 127.57 (d), 127.62 (d), 127.65 (d), 132.49 (d), 135.36 (s), 136.89 (s)	236 (M^+, 3), 105 (100)
3e (*trans*)	2.29 (dd, 1H, J = 6.8, 15.1), 2.68 (dd, 1H, J = 6.8, 15.1), 4.02 (s, 1H), 4.94 (d, 1H, J = 15.1), 4.97 (d, 1H, J = 10.3), 5.63–5.73 (m, 1H), 7.18–7.47 (m, 10H)	34.77 (t), 65.75 (s), 66.72 (d), 118.04 (t), 126.02 (d), 126.56 (d), 128.22 (d), 128.37 (d), 128.63 (d), 129.16 (d), 132.90 (d), 135.59 (s), 140.53 (s)	236 (M^+, 2), 105 (100)
3f	0.92 (t, 3H, J = 7.3), 1.64 (q, 2H, J = 7.3), 2.34 (d, 2H, J = 7.4), 2.69 (s, 2H), 5.08 (d, 1H, J = 11.3), 5.10 (d, 1H, J = 15.0), 5.57–5.96 (m, 1H)	8.75 (q), 27.07 (t), 38.66 (t), 51.31 (t), 59.48 (s), 117.72 (t), 133.15 (d)	112 (M^+, 0.6), 57 (100)
3g	0.96 (s, 9H), 2.45–2.58 (m, 3H), 2.71 (d, 1H, J = 4.9), 5.03 (d, 1H, J = 9.8), 5.04 (d, 1H, J = 19.1), 5.63–5.73 (m, 1H)	26.06 (q), 33.73 (s), 34.58 (t), 47.89 (t), 63.10 (s), 117.53 (t), 134.01 (d)	140 (M^+, 0.3), 57 (100)
8j	1.74–1.83 (m, 1H), 1.89–1.98 (m, 1H), 2.07–2.19 (m, 2H), 2.51 (dd, 1H, J = 7.8, 14.2), 2.61 (dd, 1H, J = 7.8, 14.2), 3.90 (dd, 1H, J = 5.9, 7.8), 3.98 (dd, 1H, J = 7.8, 14.7), 4.99 (d, 1H, J = 12.2), 5.00 (d, 1H, J = 15.6), 5.62–5.73 (m, 1H), 7.19–7.38 (m, 5H)	25.62 (t), 37.30 (t), 46.92 (t), 67.70 (t), 86,20 (s), 117.33 (t), 125.18 (d), 126.28 (d), 127.87 (d), 134.22 (d), 146.57 (s)	(CI) 189 ($M^+ + 1$, 83), 147 (100)
8k	1.19 (s, 3H), 1.58–1.64 (m, 1H), 1.80 (dd, 1H, J = 7.3, 12.2), 1.87–1.94 (m, 2H), 2.26 (dd, 2H, J = 1.0, 7.3), 3.84 (dd, 2H, J = 6.8, 8.3), 5.06 (d, 1H, J = 11.7), 5.07 (d, 1H, J = 15.1), 5.78–5.87 (m, 1H)	25.98 (q), 26.04 (t), 36.18 (t), 45.67 (t), 67.31 (t), 82.19 (s), 117.37 (t), 134.98 (d)	111 ($M^+ - CH_3$, 3), 85 (70), 43 (100)

not be followed by the cyclizaton, because the successive oxirane formation is allowed only in the corresponding trans form.

Next, we attempted the synthesis of allyloxetane from β-chloro ketone **2i**. However, the attempt resulted in the formation of a mixture of two homoallyl alcohols, **6i** and **7i**, as shown in Scheme 3. The formation of **7i** is probably due to the allylation of the α,β-unsaturated ketone which could be formed via the abstraction of the α-proton in **2i** by intermediate tin alkoxides **II** and **III**. On the contrary, the allylation of γ-chloro ketones proceeded successfully to give 2-allyltetrahydrofurans in moderate yields (Scheme 4).



1 **2j** R = Ph, **k** R = Me → **8j** R = Ph, 61%, **k** R = Me, 46%

Scheme 4

^{1}H NMR and ^{13}C NMR spectra were performed on a Hitachi R-90H (90 MHz) or a JEOL JNM-GSX-400 (400 MHz) spectrometer. Mass spectra were obtained with a JEOL JMS-DX303 spectrometer (HRMS data software processing, JMS-DA 5000). Analytical GLC was performed on a Shimadzu GC-8A using a 2 m × 3 mm glass column packed with Silicone SE-52 on Uniport HP (15%, 60–80 mesh). Short-path distillations of products were carried out in a Kugelrohr apparatus. All halo ketones and Et_4NCl were commercially available and were used without further purification. HMPT was freshly distilled over CaH_2. Diallyldibutyltin was prepared according to the described method.[7]

2-Allyl-2-phenyloxirane (3a); Typical Procedure:

2-Chloroacetophenone (**2aa**; 0.31 g, 2 mmol) was added to a solution of diallyldibutyltin (**1**; 0.63 g, 2 mmol) and Et_4NCl (0.03 g, 0.2 mmol) in 1,2-dichloroethane (1 mL), and the resulting mixture was stirred at 60 °C for 1 h. After the complete consumption of **2aa** monitored by GLC, Et_2O (50 mL) and aq NH_4F (10%, 50 mL) were added for the removal of organotin bromide. The yield of **3a** was determined by GLC. After the ethereal layer was dried ($MgSO_4$), **3a** was isolated by distillation.

Allyloxiranes **3a–g** were identified as shown in Table 2, and other products such as homoallyl ketone **4d** and allylcyclohexanol **5h** were identified as follows:

2-Methyl-1-phenyl-4-penten-1-one (**4d**): bp 65°C/0.1 Torr.

IR (neat): ν = 1680 (C=O), 1640 cm^{-1}(C=C).

^1H NMR ($CDCl_3$/TMS): δ = 1.24 (d, 3H, J = 7.1 Hz), 2.05–2.47 (m, 1H), 2.46–2.75 (m, 1H), 3.38–3.68 (m, 1H), 5.03 (d, 1H, J = 11.3 Hz), 5.06 (d, 1H, J = 16.5 Hz), 5.62–6.17 (m, 1H), 7.48–7.56 (m, 3H), 7.93–8.10 (m, 2H).

^{13}C NMR ($CDCl_3$): δ = 16.83 (q), 37.44 (t), 40.22 (d), 116.41 (t), 127.97 (d), 128.33 (d), 132.54 (d), 135.47 (d), 138.09 (s), 202.94 (s).

MS: m/z (%) = 174 (M^+, 13), 105 (PhCO, 100).

HRMS: m/z, $C_{12}H_{14}O$, calc.: 174.1045; found: 174.1065.

cis-1-Allyl-2-chlorocyclohexanol (**5h**): The cis configuration was attributed by ^1H NMR (an NOE spectrum).[8] Bp 65°C/2 Torr.

^1H NMR ($CDCl_3$/TMS): δ = 1.23–2.06 (m, 8H), 1.94 (s, 1H, OH, D_2O exchangeable), 2.38 (d, 2H, J = 7.3 Hz), 3.98 (dd, 1H, J = 5.4, 10.3 Hz, CHCl, *axial*-H), 5.14 (d, 1H, J = 12.2 Hz), 5.14 (d, 1H, J = 15.1 Hz), 5.77–5.87 (m, 1H).

^{13}C NMR ($CDCl_3$): δ = 20.69 (t), 25.48 (t), 32.50 (t), 34.99 (t), 45.29 (t), 68.28 (d), 72.74 (s), 118.94 (t), 132.97 (d).

MS: m/z (%) = 174 (M^+, 0.3), 133 ($M^+ - CH_2CH=CH_2$, 100).

HRMS: m/z, $C_{17}H_{16}ClO$, calc.: 174.0811; found: 174.0820.

Reaction of 3-Chloropropiophenone with Diallyldibutyltin:

3-Chloropropiophenone (**2i**; 0.34 g, 2 mmol) was added to the solution of **1** (0.63 g, 2 mmol) and Et_4NCl (0.03 g, 0.2 mmol) in 1,2-dichloroethane (1 mL), and the resulting mixture was stirred at 80°C for 3 h. After the reaction, Et_2O (50 mL) and aq NH_4F (10%, 50 mL) were added for the removal of organotin chloride. The yields of chlorohexenol **6i** and hexadienol **7i** were determined by GLC. After the ethereal layer was dried ($MgSO_4$), **6i** and **7i** were isolated by column chromatography on silica gel, then purified by distillation, and identified as follows:

1-Chloro-3-phenyl-5-hexen-3-ol (**6i**): bp 90°C/0.1 Torr.

$C_{12}H_{15}ClO$	calc.	C 68.40	H 7.18	Cl 16.83
(210.7)	found	68.68	7.03	16.52

^1H NMR ($CDCl_3$/TMS): δ = 2.22 (s, 1H, OH, D_2O exchangeable), 2.33 (t, 2H, J = 8.3 Hz), 2.56 (t, 2H, J = 8.8 Hz), 3.10–3.77 (m, 2H), 5.16 (d, 1H, J = 15.5 Hz), 5.18 (d, 1H, J = 11.3 Hz), 5.38–5.73 (m, 1H), 5.38 (s, 5H).

^{13}C NMR ($CDCl_3$): δ = 40.10 (t), 45.47 (t), 47.76 (t), 75.17 (s), 120.35 (t), 124.90 (d), 126.85 (d), 128.28 (d), 132.40 (d), 144.26 (s).

MS: m/z (%) = 169 ($M^+ - CH_2CH=CH_2$, 100).

3-Phenyl-1,5-hexadien-3-ol (**7i**): bp 60°C/0.1 Torr.

^1H NMR ($CDCl_3$/TMS): δ = 2.18 (s, 1H, OH, D_2O exchangeable, 2.72 (d, 2H, J = 7.3 Hz), 5.08–5.39 (m, 4H), 5.49–5.94 (m, 1H), 6.21 (dd, 1H, J = 10.5, 17.3 Hz), 5.24–5.50 (m, 5H).

^{13}C NMR ($CDCl_3$): δ = 46.60 (t), 75.68 (s), 112.91 (t), 119.62 (t), 125.26 (d), 126.72 (d), 128.04 (d), 133.01 (d), 143.46 (d), 144.99 (s).

MS: m/z (%) = 174 (M^+, 0.1), 133 ($M^+ - CH_2CH=CH_2$, 100).

HRMS: m/z, $C_{12}H_{14}O$, calc.: 174.1045; found: 174.1058.

2-Allyl-2-phenyltetrahydrofuran (8j); Typical Procedure:

4-Chlorobutyrophenone (**2j**; 0.37 g, 2 mmol) was added to the solution of **1** (0.63 g, 2 mmol) and Et_4NCl (0.03 g, 0.2 mmol) in 1,2-dichloroethane (1 mL), and the resulting mixture was stirred at 80°C for 22 h. Then, Et_2O (50 mL) and aq NH_4F (10%, 50 mL) were added for the removal of organotin bromide. The yield of allyltetrahydrofuran **8j** was determined by GLC. After the ethereal layer was dried ($MgSO_4$), **8j** was isolated by distillation, and identified as showed in Table 2.

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(8) The presence of NOE enhancement between allylic CH_2 and ring CHCl confirmed the stereochemistry of the cis isomer.