

단 신

Cp₂TiCl₂를 촉매로 한 LiBH₄에 의한 *gem*-Dibromocyclopropanes의
Cyclopropanes으로의 탈브롬화반응

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Cp₂TiCl₂ Catalyzed Debromination of *gem*-Dibromocyclopropanes
to Cyclopropanes by LiBH₄

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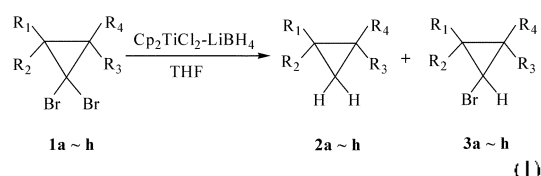
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INTRODUCTION

The reduction of halogen derivatives of hydrocarbons is very efficient and reliable procedure in organic synthesis, and a number of reducing agents for this have been reported.¹ For dehalogenations, *gem*-dihalocyclopropanes have been shown to be extremely valuable starting materials for the preparation of cyclopropane and cyclopropene derivatives.² The reduction of *gem*-dihalocyclopropanes to monohalocyclopropanes has been effected by various reducing reagents such as organotin hydride,^{3a} Grignard reagent,^{3b} chromium sulfate,^{3c} lithium aluminum hydride,^{3d,e} sodium borohydride,^{3f} potassium diphenyl phosphide,^{3g} sodium hydrogen telluride,^{3h} and silver perchlorate.³ⁱ Titanium complexes serve as a catalyst for the dehalogenation such as the reduction of aromatic halides with NaBH₄,^{4a,b} the dehalogenation of organic halides by RMgX,^{4c} the defluorination of perfluorodecalin by using Al/HgCl₂,^{4d} and the dehalogenation of monohalopyridines with Red-Al.^{4e} The reductive debromination of *vic*-dibromides to alkenes by using Cp₂TiCl₂/Zn combination reagent^{5a} or Cp₂TiCl₂/In system^{5b} was also

reported. Cp₂ZrCl₂ has been used for the catalytic dehalogenation of aromatic halides by alkylmagnesium reagents^{6a} and the stoichiometric hydrolysis of aromatic perfluorocarbons using Mg/HgCl₂.^{6b} However, these methods have not been achieved for the direct conversion of *gem*-dibromocyclopropanes to cyclopropane as a practical method. During the course of our studies on reactions of unsaturated hydrocarbons catalyzed by titanium or zirconium complexes,⁷ we found the debromination of *gem*-dibromocyclopropanes with LiBH₄ to cyclopropanes catalyzed by Cp₂TiCl₂ in THF (eq. 1).



EXPERIMENTAL SECTION

All glassware used was predried in an oven, assembled hot and cooled with a stream of argon in glove box. All reactions were carried out under

argon atmosphere. All solvents were distilled and stored over an appropriate drying agent. Cp_2TiCl_2 , LiBH_4 , NaBH_4 , and LiAlH_4 were purchased from Strem Co., and used without further purification. Other reagents were purified before use. ^1H NMR spectra were recorded in CCl_4 on Varian Gemini-200 spectrometer with tetramethylsilane as an internal standard. Infrared spectra were measured in a KBr pellet with a Matterson Genesis FT-IR II spectrophotometer. GC analyses were carried out with a Younglin GC-600D gas chromatograph equipped with HP-5 (Hewlett Packard, 0.32 mm, 30 m) capillary columns. Mass spectra were obtained using a Shimadzu GC/MS QP-5050.

Preparation of 1,1-dibromo-2,2-diphenylcyclopropane. A mixture of 1,1-diphenylethene (10.48 g, 58.0 mmol), bromoform (30.33 g, 120.0 mmol), and *N,N*-dimethyl-*n*-dodecylamine (0.239 g, 1.12 mmol) was stirred in benzene (15 mL). 50% Sodium hydroxide (80 mL) was added dropwise to the solution, the reaction mixture was stirred vigorously at 50 °C for 4 h. The mixture was treated with dilute hydrochloric acid (100 mL) and extracted with diethyl ether/benzene(1/1) (3/30 mL). The organic layer was dried over magnesium sulfate, and the solvent was removed under reduced pressure. Recrystallization of the product from benzene gave 1,1-dibromo-2,2-diphenylcyclopropane (11.3 g, 55%), mp. 154~156 °C, ^1H NMR (CCl_4): δ 7.14~7.46 (m, 10H, Ar), 2.39 (s, 2H, CH_2), IR (cm^{-1}): 3029, 1595, 1446, 1162, 669. Mass m/e 350 (M^+), 352 (M^+-2), 354 (M^++4).

gem-Dibromocyclopropanes were prepared from

appropriate alkenes and dibromocarbene by the reported procedure.⁹

Typical procedure for debromination of 1,1-dibromo-2-phenylcyclopropane to phenylcyclopropane. The mixture of Cp_2TiCl_2 (1.01 g, 4.04 mmol), LiBH_4 (0.894 g, 41.1 mmol), and THF (25 mL) was placed in a vessel under argon. After stirring for 1 h, and 1,1-dibromo-2-phenylcyclopropane (4.40 g, 15.9 mmol) in THF (15 mL) was slowly introduced to the mixture at 40 °C. The complete reaction was confirmed by GC, and the mixture was treated with dilute hydrochloric acid (20 mL) and extracted with diethyl ether. The organic layer was dried over sodium sulfate, and the solvent was evaporated under reduced pressure. The residue was purified by column chromatography on silica-gel with *n*-hexane (1.13 g, 60 %). The distillation of the residue gave phenylcyclopropane under reduced pressure (bp. 62~63 °C/13 mm). ^1H NMR (CCl_4): δ 7.08~7.23 (m, 5H, Ar), 1.70~2.51 (m, 1H, CH), 0.62~1.10 (m, 4H, CH_2), IR (cm^{-1}): 3028, 1595, 1446, 1162, 729, 699.

The products are already reported (in the literature) and were characterized by comparison with authentic samples using GC and spectral data.

RESULTS AND DISCUSSION

The debromination of 1,1-dibromo-2-phenylcyclopropane (**1a**) in the presence of catalytic amounts of Cp_2TiCl_2 was examined in THF under various reaction conditions (Table 1). In the reaction of **1a** (4.1 mmol) with LiBH_4 (10.1 mmol) in THF (15 mL) in the absence of Cp_2TiCl_2 at 25 °C for 5 h, phenyl-

Table 1. Debromination of **1a** catalyzed by Cp_2TiCl_2 under various conditions^a

Catalyst	Reducing agent	Solvent	Temp. (°C)	Time (h)	Yield(%) ^b	
					2a	3a
none	LiBH_4	TUF	25	5	-	-
none	LiBH_4	TUF	65	5	-	18
Cp_2TiCl_2	LiBH_4	TUF	25	48	92	3
Cp_2TiCl_2	LiBH_4	TUF	40	5	87	-
Cp_2TiCl_2	LiBH_4	TUF	65	5	76	15
Cp_2TiCl_2	NaBH_4	DMF	40	24	trace	trace
Cp_2TiCl_2	NaBH_4	diglyme	40	24	trace	trace
Cp_2TiCl_2	LiAlH_4	TUF	40	5	76	20

^aCatalyst: reducing agent : **1a** = 1 : 10 : 4. ^bGC yields.

cyclopropane (**2a**) was not obtained and **1a** was mostly recovered, but 1-bromo-2-phenylcyclopropane (**3a**) was obtained in 18% yield at 65 °C for 5 h. Addition of catalytic amounts of Cp₂TiCl₂ (1.1 mmol) to the mixture of **1a** and LiBH₄ in THF promoted the debromination of **1a** to **2a** at 25 °C, but the reaction proceeded very slowly (48 h). The reaction of **1a** occurred smoothly at 40 °C for 5 h to give **2a** as a major product in an excellent yield, but **2a** and **3a** were obtained at 65 °C for 5 h in 76% and 15% yields, respectively. The reaction of **1a** with equimolar amounts of Cp₂TiCl₂ afforded **2a** in 98 % yield without formation of the expected coupling products.^{4c} The reduction of aryl halides with NaBH₄ catalyzed by Cp₂TiCl₂ was reported to be solvent dependent.^{4b} Therefore, we examined the debromination of **1a** to **2a** with NaBH₄ at 40 °C in DMF and diglyme, respectively, but these reactions were not achieved under the same reaction conditions. The reactions required long reaction times or elevated temperatures.^{4a,b} The similar reduction of **1a** with LiAlH₄ instead of LiBH₄ was tested. **2a** and **3a** were obtained in 76% and 20% yields, respectively. The selectivity of Cp₂TiCl₂-LiAlH₄ system shows poorer than that of Cp₂TiCl₂-LiBH₄ system for the reduction of *gem*-dibromocyclopropanes to cyclopropanes. The debromination of *gem*-dibromocyclopropanes with LiBH₄ catalyzed by Cp₂TiCl₂ in THF at 40 °C was found to be superior and selectively proceeded to give cyclopropanes. The results are listed in Table 2. As shown in Table 2, the debromination of *gem*-dibromocyclopropanes with phenyl groups (**1a**~**1c**) occurred to give the corre-

sponding cyclopropanes in an excellent yields, but the yields of cyclopropanes with *p*-tolyl and alkyl groups (**1d**, **1e**) were low and monobromocyclopropanes (**3d**, **3e**) were little obtained with recovery of the substrates in high yields. The product yields are considerably affected by the electronic nature of substituents on the *gem*-dibromocyclopropanes. The reduction of *trans*-**1c** was achieved to give *trans*-**2c**. The debromination of **1g** and **1h** smoothly proceeded without a cleavage of C-O bond. The debrominations are chemoselective as ether and ester groups remained unaffected under the reaction conditions.^{5b,6a} Also, the dechlorination of 1,1-dichloro-2,2-diphenylcyclopropane was applied to this reagent system. This reaction hardly occurred under the same conditions, and required a elevated temperature (65 °C) and a longer time to complete the reaction (>48 h).^{4a} Deuterolysis after the reaction of **1b** with LiBH₄ did not give any trace of deuterated 1,1-diphenylcyclopropanes, but the reaction of **1b** with LiBD₄ gave dideuterated 1,1-diphenylcyclopropane. The source of hydrogen in this reaction should be derived from LiBH₄. The reaction mechanism is not clear yet. However, we would like to consider possible paths on Cp₂TiCl₂ catalyzed debromination of *gem*-dibromocyclopropanes by LiBH₄. One involves a oxidative addition/reductive elimination to the low valence titanium complex species.⁶ Another possible path is a radical reaction involving reduced titanium complex catalysts.^{4b} Although the role of Cp₂TiCl₂ is still not clarified, it is likely that reduction of Cp₂TiCl₂(IV) with LiBH₄ provides low valent titanium, which reacts with *gem*-dibromocyclopro-

Table 2. Debromination of *gem*-dibromocyclopropanes^a

Substrate	Dibromocyclopropane				Yield(%) ^b	
	R ₁	R ₂	R ₃	R ₄	2	3
1a	C ₆ H ₅	H	H	H	87(60)	-
1b	C ₆ H ₅	C ₆ H ₅	H	H	95	-
1c ^c	C ₆ H ₅	H	C ₆ H ₅	H	92(67)	-
1d	<i>p</i> -CH ₃ C ₆ H ₄	H	H	H	42	<5
1e	H	(-Cl) ₂ -	H	H	38	<5
1f	C ₆ H ₅	Cl	H	H	78	<3
1g	Cl	CH ₂ OC ₆ H ₅	H	H	92	-
1h	Cl	COOEt	H	H	76	-

^aCp₂TiCl₂ : LiBH₄ : substrate = 1 : 10 : 4, 40 °C, 5 h. ^bGC yields, isolated yields in parenthesis. ^c*Trans* type.

panes to give cyclopropanes.⁹ The actual reaction might be further complicated with multiple paths. Although the scope and limitations were not fully established, the present method could be a practical alternative to conventional method.

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