



A Facile Conversion of Substituted Cyclobutanones to Cyclopentanones by $\text{CH}_2\text{I}_2/\text{SmI}_2$ System

Shin-ichi Fukuzawa * and Teruhisa Tsuchimoto†

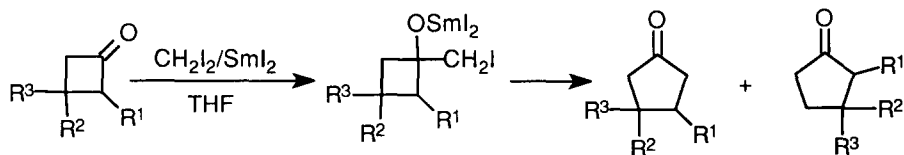
Department of Applied Chemistry, Chuo University, Bunkyo-ku, Tokyo 112, Japan

Abstract: Ring expansion reaction of a substituted cyclobutanone with CH_2I_2 and SmI_2 proceeded cleanly in extended reaction time (15 h) to afford the corresponding cyclopentanone in good yield, whereas short reaction time (0.5 h) produced a mixture of iodohydrin and cyclopentanone.

Cyclobutanone derivatives are a precursors choice in synthesizing cyclopentanone derivatives, among which are biological and pharmacological importance. Several transformation methods of cyclobutanones to cyclopentanones have been developed to date. Homologation and ring enlargement of cyclobutanones with diazomethane is one of the efficient ways.¹⁾ Tiffeneau-Demjanov rearrangement of amino alcohols, which were prepared by the reduction of cyclobutanone cyanohydrins, is an alternative method which avoids use of toxic and dangerous diazomethane.²⁾ Another method is a thio- or selenomethylation of cyclobutanones and subsequent rearrangement of β -thio- or selenomethylcyclobutanols.³⁾

Samarium diiodide (SmI_2)-induced iodomethylation of ketones and aldehydes with diiodomethane provides a simple and valuable way for synthesis of iodohydrins.⁴⁾ Cycloalkanone halohydrins undergo a ring expansion reaction when exposed to a base.⁵⁾ The iodomethylation reaction has attracted interest in the transformation method of cyclobutanones to cyclopentanones. In this report, we present a facile, one pot synthesis of cyclopentanones from cyclobutanones by the reaction with diiodomethane and SmI_2 under neutral conditions, which involves an iodomethylation and rearrangement sequence.

On treatment of substituted cyclobutanones with CH_2I_2 and SmI_2 in THF at room temperature for 15 h, the ring expansion reaction proceeded cleanly to afford the corresponding cyclopentanones in good to excellent yields. On the other hand, when the reaction was quenched just after the green color of divalent samarium faded (usually within 30 min), the products were a mixture of iodohydrins and cyclopentanones. These results are summarized in Table 1.



3-Monosubstituted and 3,3-disubstituted cyclobutanones are examined because of the easiness of preparation (Table 1, entries 1-8).⁶⁾ Reaction time less than 10 h was insufficient to complete rearrangement reaction, and at shorter reaction time the product would be contaminated by iodohydrin. Thus, reaction time must be extended to obtain cyclopentanones selectively as a sole product. With bicyclic cyclobutanone two regioisomers of cyclopentanone derivatives were produced (Table 1, entries 9-13).

† Graduate student from Tokyo Institute of Technology, Japan

Table 1. SmI₂ induced Reaction of Cyclobutanone with CH₂I₂ ^{a)}

Entry	Cyclobutanone			Time (h)	Product (s) and Yield (%) ^{b)}	
	R ¹	R ²	R ³		Iodohydrin	Cyclopentanone
1	H	Ph	H	0.5	44	16
2	H	Ph	H	15	trace	61
3	H	n-Bu	H	0.5	34	41
4	H	n-Bu	H	15	trace	88
5	H	tert-Bu	H	0.5	22	32
6	H	tert-Bu	H	15	trace	53
7	H	Me	Ph	0.5	47	16
8	H	Me	Ph	15	trace	65
9	-(CH ₂) ₄ -		H	15	trace	40 ^{c)}
10	-CH ₂ CH=CHCH ₂ -		H	15	trace	52 ^{c)}
12	-(CH ₂) ₅ -		H	0.5	trace	73 ^{d)}
13	-(CH ₂) ₅ -		H	15	trace	82 ^{d)}

a) SmI₂ (2.1 mmol, 0.1 M solution of THF), Cyclobutanone (1.0 mmol), CH₂I₂ (1.0 mmol). b) Isolated yield. c) Approximately 1:1 mixture of the regioisomers. d) Isomer ratio of the regioisomers is 97:3.

The following outlines a typical experimental procedure for 3-phenylcyclobutanone. To a THF solution of SmI₂ (0.1 M, 2.1 mmol) was added a mixture of CH₂I₂ (1.0 mmol) and 3-phenylcyclobutanone (1.0 mmol) at room temperature. The solution was stirred for 15 h. After usual workup, the product was isolated by column chromatography, and analytical data agreed with its structure.

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