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Photochemical and radical initiator-induced reaction of allylic indium compounds

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Abstract—Intramolecular cyclization of allylic radicals generated from allylindium compounds both by photolysis or by the reaction of radical initiators was examined. The photolysis of allylic indium compounds, prepared from 8-bromo- or 8-iodooct-1,6-dienes and powdered indium metal, led to the formation of the 5-*exo*-trig products. Benzoyl peroxide as a radical initiator was also effective for the cyclization. In contrast, the radical initiators with oxidizing nature, such as *tert*-butyl hypochlorite, induced iodocyclization producing iodomethylcyclopentane via an oxidation of the iodide on the indium atom.

1. Introduction

Organoindium compounds have hitherto been developed as nucleophilic reagents in organic synthesis.[1] Addition to the unsaturated bond in carbonyl compounds and imines is a typical reaction of allylindium reagents, giving the corresponding homoallylic alcohols and amines, respectively. Alkynes,[2] allenes,[3] and cyclopropenes[4] also undergo allylindation to afford allylated products, where a suitably introduced hydroxy group exerts a significant effect for both acceleration and stereoselectivity of the allylation. However, an addition to carbon–carbon double bonds without a proper activation, such as substitution by electron-withdrawing groups[5] or introduction of a hydroxy group adjacent to the double bond,[6] has not been attained owing to the low nucleophilicity of organoindium compounds. Recently, indium-mediated radical reactions have been reported, involving single electron transfer (SET) reactions caused by metallic indium or reactions of organoindium reagents with organic radicals.[7] Although photolysis of organometallic compounds leading to organic radicals is documented for organocobalt compounds,[8] photochemical reactions dealing with organoindium compounds remains unexplored. Here we first report a generation of organic radicals by a photolytic cleavage of a carbon–indium bond in organoindium compounds and subsequent intramolecular additions to carbon–carbon double bonds. A similar reaction mediated by radical initiators was also examined to compare with the photochemical reaction.

2. Photochemical reactions

Diene **1a** and indium were refluxed in THF for 3 h giving allylic indium **A**, which was then irradiated with a high-pressure mercury lump (100 W, Pyrex filter) in THF to afford the 5-*exo*-cyclization product **2** in 51% yield (entry 1, Table 1). The corresponding 6-*endo*-cyclization product was not obtained. In order to estimate the amount of **2** formed via a pyrolytic course, the allylic indium compound **A** was quenched with 1 N HCl prior to the irradiation, leading to the corresponding protonated product **3** in 11% yield together with a small amount of **2** (3%) (entry 2). These results indicate that the present cyclization was induced by the photolysis of **A** and the thermal decomposition is negligible. The protolysis of allylindium compounds generally proceeds selectively at the γ-position to give the corresponding protonated products in good yields.[9] The low yield of **3** in entry 2 may be attributed to a decomposition/polymerization of **A** in a significant amount under the refluxing conditions. Therefore, the allylic indium compound was next prepared at room temperature by changing bromide **1a** to the more reactive iodide **1b**. The disappearance of metallic indium was observed by mixing

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Keywords: Indium; Radical; Photolysis; Cyclization.

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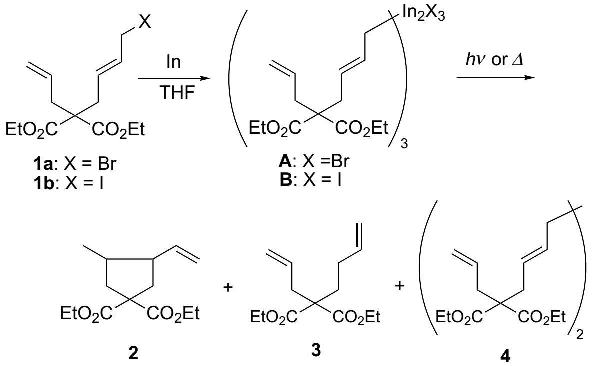
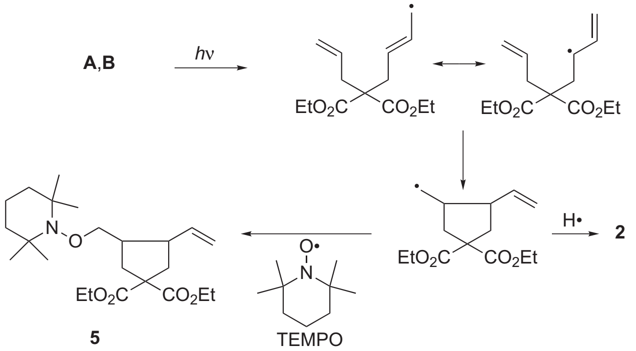
Table 1. Intramolecular cyclization of allylindium compounds **A**, **B**



Entry	Substrate	Conditions	Products and yield (*cis*:*trans*)
1	**1a**	rfx, 3 h → *hv*, rt, 36 h	**2**: 51% (85:15)
2	**1a**	rfx, 4 h	**2**: 3%, **3**: 11%
3	**1b**	rt, 2 h → *hv*, rt, 24 h	**2**: 34% (93:7), **4**: 24%
4	**1b**	rt, 2 h	**3**: 18%, **4**: 10%
5[a]	**1a**	rt, 2 h → *hv*, rt, 20 h	**2**: 16% (57:43), **4**: 61%

[a] With LiI.

1b at room temperature for 2 h, and the resulting solution was irradiated for 24 h to produce **2** in 34% yield together with the dimer **4** in 24% yield (entry 3). Quenching **B** by 1 M HCl furnished protolysis product **3** in 18% yield and the dimer **4** in 10% yield (entry 4). The reaction of allylic indium derived from **1a** in the presence of LiI at room temperature gave rise to the dimer **4** predominantly (61% yield) and **2** was obtained only in 16% yield (entry 5). Although the reasons are unclear for the increase of the yield of **4** and for the decrease of the stereoselectivity of **2** in entry 5, the above results show that refluxing during the preparation of the allylic indium reagents is not responsible for the diminution in the yield of **2**. The chemical nature of **A** is distinct from conventional allylic indium reagents; for example, the reaction of **A** with benzaldehyde did not give the corresponding homoallylic alcohol at all.

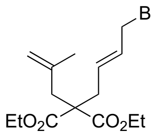
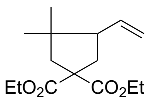
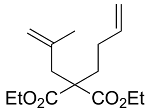
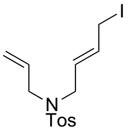
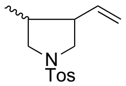
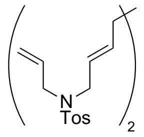
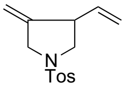


Scheme 1. Possible mechanism for the photochemical radical cyclization.

The most plausible mechanism is depicted in Scheme 1; the irradiation of **A** or **B** causes a homolytic cleavage of the In–C bond and the resulting radical attacks the carbon–carbon double bond intramolecularly in a 5-*exo*-trig fashion leading to the cyclopentylmethyl radical, which abstracts hydrogen from the solvent THF to produce **2**. The presence of the radical intermediate was confirmed by an experiment using 2,2,6,6-tetramethylpiperidin-1-oxyl (TEMPO):[10] the photolysis of allylic indium **A** in the presence of TEMPO gave **5** in 17% yield.

Next, similar dienes **6** and **7** were subjected to the photochemical intramolecular cyclization reaction under the identical conditions. The results are summarized in Table 2. Diene **6**, in which a methyl group was introduced at the reactive site, also gave the corresponding

Table 2. Photochemical reaction of allylic indium compounds derived from **6** and **7**[a]

Entry	Substrate	*t* (h)	Product and yield (%)	
1	 **6**	23	 **8**:33	 **9**:6
2	 **7**	20	 **10**:42 (51:49)[b]	 **11**:19
3[c]	**7**	22	**10**:32 (63:37)[b]	 **12**:4

[a] Allylindium compounds, prepared from diene **6** or **7** in THF at reflux, were irradiated in THF (30 mL).

[b] Diastereomeric ratio in the crude product.

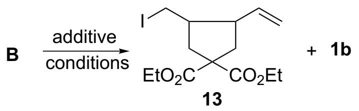
[c] InI was used instead of In.

cyclization product **8** in moderate yield (entry 1, Table 2). In the case of tosyl amide **7**, the 5-*exo*-cyclization product **10** was formed in 42% yield along with the dimer **11** in 19% yield (entry 2). When the allylic indium compound prepared with InI in place of In gave **10** in 32% yield with a small amount of the dehydrogenated product **12** (4% yield).

3. Radical initiator-induced reactions

The reaction of oraganoindium compounds with organic radicals provides a new organic radicals.[7e] To compare with the above-mentioned photo-induced radical cyclization, the radical initiator-mediated reaction of allylic indium **B** was performed. A solution of **B** in THF was treated with *tert*-butyl hypochlorite at 60 °C to give iodomethylcyclopentane **13** in 37% yield as a single diastereomer (entry 1, Table 3). The cyclization product **2** obtained in the photochemical reaction was not found. It is noted that the starting iodide **1b** was obtained in 11% yield, although **1b** disappeared completely after the preparation of **B**. As the source of iodine atom in **13** is restricted to the iodide of the allylic indium sesquiiodide **B**, **1b** is considered to be reproduced from **B**. These phenomena were closely resemble to the iodination of cyclopropylindium,[11] where the iodine atom on the indium is transferred to the cyclopropane in the presence of oxidants, such as *tert*-butyl hypochlorite and *N*-chlorosuccinimide (NCS). It is considered that the iodide on the indium atom was oxidized to iodonium ion, which attacked the terminal olefin bond of **B** (**B′**) and the resulting iodonium intermediate underwent the intermolecular cyclization to give **13** (Scheme 2). The reactions of allylic indium **B** were examined by changing the oxidizing agents. The results are summarized in Table 3.

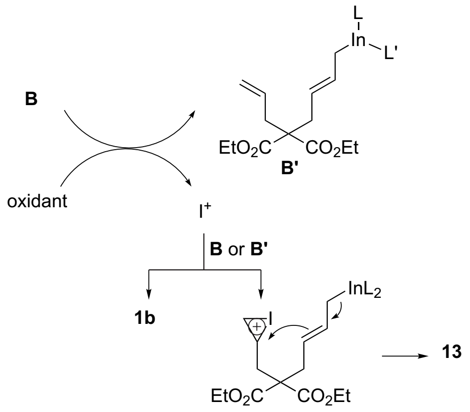
Table 3. Iodocyclization of the allylic indium compound **B**



Entry	Additive (mol%)	*T*	*t* (h)	Yield (%)	
				13	**1b**
1	*t*-BuOCl (150)	60 °C	2	37	11
2	*t*-BuOCl (200)	60 °C	5	53	0
3[a]	*t*-BuOCl (200)	60 °C	5	47	0
4	*t*-BuOCl (200)	rt	3	31	17
5[b]	*t*-BuOCl (200)	60 °C	2	35	Trace
6	*t*-BuOCl (200), TEMPO (200)	60 °C	2	29	Trace
7	*t*-BuOCl (200), galvinoxyl (140)	60 °C	2	11	0
8	BPO (300)	rt	20	39	5
9	BPO (300), TEMPO (200)	rt	22	35	6
10	$K_3[Fe(CN)_6]$ (400)	rt	63	28	0
11	NCS (200)	60 °C	2	32	5
12	NIS (200)	60 °C	15	13	17
13	I_2 (200)	rt	16	0	15
14	—	rfx	14	26	Trace

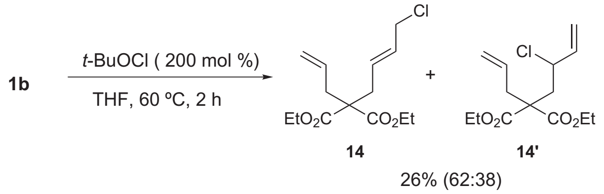
[a] DMF was used instead of THF.

[b] InI was used instead of In.



Scheme 2. Possible mechanism for the iodocyclization.

By prolonging the reaction time to 5 h, *tert*-butyl hypochlorite gave **13** exclusively in 53% yield (entry 2). The same reaction in DMF also proceeded (entry 3). The reaction performed at room temperature increased the ratio of **1b** (entry 4). Allylic indium derived from InI also gave the cyclization product **13** (entry 5). The reaction in the presence of TEMPO or galvinoxyl gave **13** (entries 6 and 7), indicating that the reaction proceeded via an ionic path. Other oxidizing agents, such as benzoyl peroxide (BPO), potassium ferricyanide, NCS, and *N*-iodosuccinimide (NIS), were also effective for the iodocyclization (entries 8–12). With I_2, no cyclization occurred (entry 13). Refluxing of **B** in THF without additives gave **13** in 26% yield (entry 14), showing that an ionic cleavage of In–I bond in **B** occurred also by pyrolysis. Exposure of **1b** to *tert*-butyl hypochlorite gave a mixture of the chlorinated products **14** and **14′** (26%, **14**:**14′** = 62:38), and **13** was not formed; therefore, **13** is considered to be formed via allylic indium **B**, and not directly from **1b** and *t*-BuOCl.



Consequently, treatment of allylic indium **B** with oxidizing agents caused the iodocyclization. In order to suppress the oxidation of the iodide on the indium atom, the reactions of allylindium **A**, derived from allylic bromide **1a**, with other radical initiators such as Et_3B were examined (Table 4). To a solution of allylic indium **A**, Et_3B was added and the mixture was stirred at room temperature, giving **2** and **3** in low yields (entry 1). The yield of **2** scarcely increased by increasing the reaction time (entry 2). As the amounts of **2** obtained in entries 1 and 2 were coincident to that formed during the preparation of **A** as is shown in Table 1, it is concluded that the radical cyclization did not proceed by the combinational use of allylic indium **A** and Et_3B. On the

Table 4. Reaction of allylic indium compound **A** with radical initiators

$\mathbf{A}$ (or $\mathbf{1a}$) $\xrightarrow[\text{conditions}]{\text{initiator}}$ $\mathbf{2}$ + $\mathbf{3}$

Entry	Initiator (mol%)	Conditions	Yield (%)	
			2 (*cis*:*trans*)	**3**
1	Et_3B (10)	30min, rt	5	1
2	Et_3B (100)	5h, rt	8	3
3	BPO (150)	rfx, 14h	57 (85:15)	0
4[a,b]	BPO (150)	rfx, 14h	25 (44:56)	0
5	AIBN (150)	rfx, 5h	Trace	0
6	$(t\text{-BuO})_2$ (150)	rfx, 16h	0	0

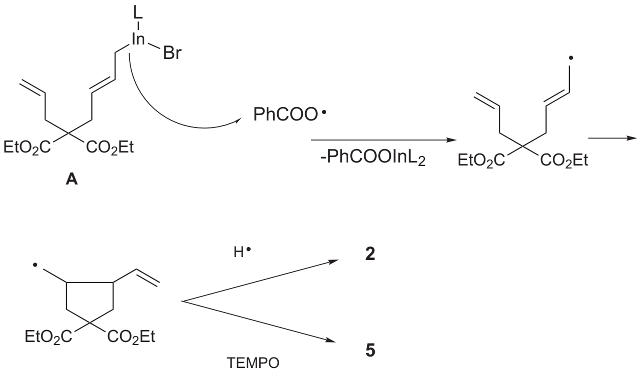
[a] Reaction of **1a** without indium.

[b] The starting bromide **1a** was recovered (71%).

other hand, when allylic indium **A** was refluxed with BPO for 14h, **2** was formed in 57% yield (entry 3), albeit the reaction of **B** led to the formation of **13** even at room temperature (entry 8, Table 3). Heating of allylic bromide **1a** with BPO led to the formation of **2** in 25% yield and the rest of **1a** was recovered (entry 4). This fact indicates that the radical cyclization proceed from both **1a** and allylic indium **A**, and the latter is much faster than the former. As initiators, 2,2′-azobisisobutyronitrile (AIBN) and di-*tert*-butyl peroxide were not effective for the cyclization (entries 5 and 6).

A plausible reaction mechanism is illustrated in Scheme 3. Benzoyl radical abstracts indium from **A** to liberate the allyl radical, which undergoes the intramolecular cyclization, as the case of photochemical reaction, giving the cyclopentylmethyl radical. This radical intermediate could be trapped by TEMPO to give **5** in 57% yield.

In summary, a homolytic cleavage of the C–In bond in allylic indium compounds was realized by both photolysis and by the action of radical initiators, and the resulting allylic radicals undergo the intramolecular cyclization in a 5-*exo*-trig mode to afford vinylcyclopentanes. When initiators with oxidizing nature, such as *tert*-butyl hypochlorite, BPO, and NCS, were involved, the intramolecular iodocyclization of the allylic indium sesquiiodide occurred via oxidation of the iodide in the allylic indium compound. Although organic stannanes have hitherto been used as a radical source, their use should be avoided in view of green chemistry. The present radical process by means of photochemical and radical initiator-induced reactions of allylindium compounds can serve as another radical process and expands the possibility of the organoindium chemistry. Further application of other organic indium compounds is currently underway.



Scheme 3. Possible mechanism for the radical initiator-induced radical cyclization.

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