Homoallyl-Substituted Vinylcyclopropanes from α,β-Unsaturated Ketones and Allylindium Derivatives[**]

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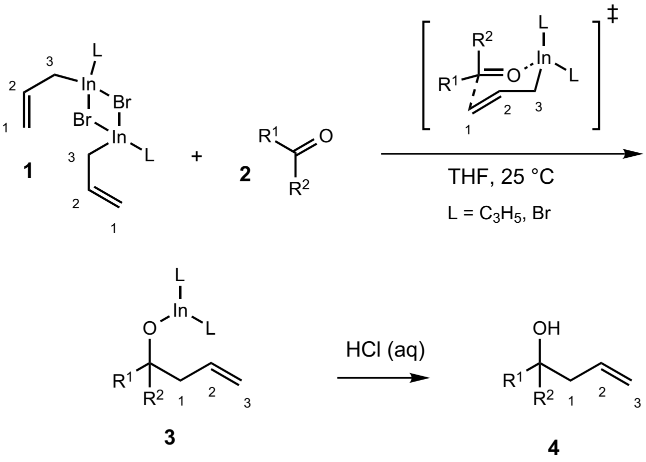
Organoindium species are of particular appeal as reagents for organic synthesis because they are often stable under aqueous and even mildly acidic conditions and are compatible with many organic functional groups.[1] Allylindium sesquihalides (allyl)$_3$In$_2$X$_3$ and dihalides (allyl)$_2$In$_2$X$_4$ **1**, prepared by the reaction of allyl halides with indium metal[2] or indium halides,[3] react smoothly with aldehydes and ketones[4] **2** via transition states of the Zimmermann–Traxler type to afford indium alkoxide intermediates **3** (Scheme 1). Hydrolysis yields homoallylic alcohols **4**.[5] Here we report on the reaction of **1** with α,β-unsaturated ketones or aldehydes **5** to produce homoallylic indium alkoxide intermediates **6**, which can be induced to undergo a deoxygenative rearrangement that results in vinylcyclopropane derivatives of type **7** (Scheme 2).



Scheme 1. Reaction of allylindium sesquibromide **1** with ketones **2** to give **3** and **4** via a Zimmerman–Traxler transition state.

In initial experiments, dibenzylideneacetone **5a** was allowed to react under nitrogen with freshly prepared (C$_3$H$_5$)$_3$In$_2$Br$_3$ (**1**) in anhydrous THF at 25 °C (**5a**:In = 1:1). After the mixture was diluted with Et$_2$O, worked up with 1 M HCl, and subjected to column chromatography, we obtained analytically pure **7a** in yields of 40–60%.[6] Thus, a reaction took place that did not lead to **8a**, but instead resulted in cleavage of the C–O bond. Presumably this involved coupling between the allylindium moiety (C(4)–C(6)) in **6a** and the C(3) terminus of the initially transferred allyl group (C(1)–C(3)) to afford the homoallyl-substituted vinylcyclopropane derivative **7a**. The overall reaction therefore involves deoxygenative sequential transfer of six carbon atoms (two allyl moieties) from the indium sesquihalide species **1** to the α,β-unsaturated ketone **5a**. A three-membered ring is formed by linkage of the carbonyl carbon atom with C(1) and C(2) of the first allyl unit. After many experiments it became clear that removal of the THF[7] (which presumably stabilizes the intermediate) and exposure of the crude product to air in an acidic medium[8] (which may induce homolysis of the C–In bond, possibly by insertion of O$_2$) is essential for efficient and reproducible diversion of **6** to **7** rather than to **8**.

We suspected that rearrangement of **6** to **7** might involve the reaction of CH$_2$=CHCH$_2$In(L)$_x$ with aerobic oxygen to afford an intermediate of the type CH$_2$=CHCH$_2$(O)$_n$In(L)$_x$ (n = 1,2). The following experiments were performed to circumvent the requirement of exposure to air. One equivalent of (C$_3$H$_5$)$_2$In$_2$I$_4$, in which each indium atom bears only one allyl group, was allowed to react with **5a** (THF, 25 °C,

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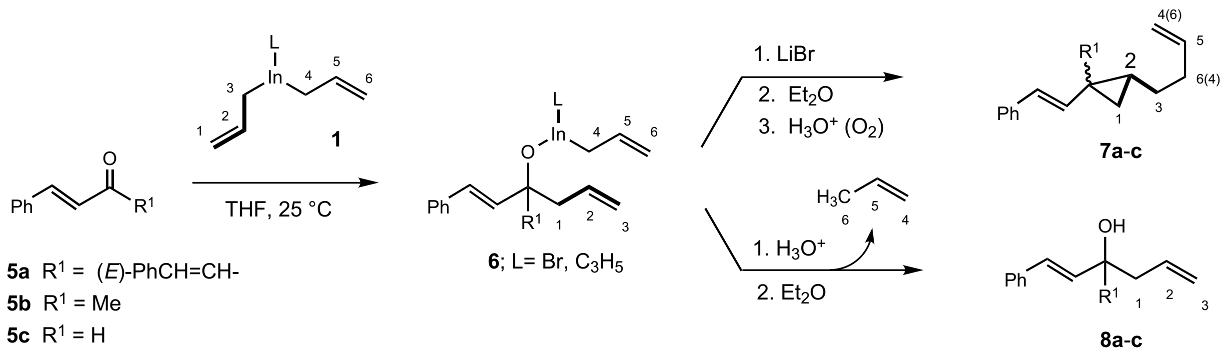
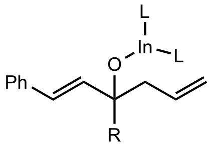
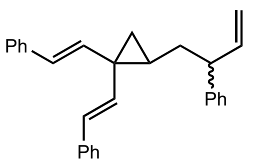

Scheme 2. Acid-catalyzed rearrangement of intermediate **6** to homoallyl-substituted vinylcyclopropane **7** and hydrolysis to **8**.

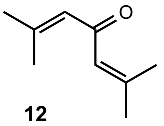
30 min) to generate **9a**, and then two equivalents of $CH_2{=}CHCH_2ONa$ were added to exchange iodide with allyl alkoxide and yield **10a** + NaI (or the corresponding indium "ate" complex).[2b, 5d] After removal of the THF the residue was stirred in toluene (18 h), and **7a** was isolated in 83 % yield after workup. However, analogous reactions with (*E*)-$PhCH{=}CHCH_2ONa$ afforded only **7a**, and not **11a**; this demonstrates that allylic moieties of the alkoxides are not incorporated. Hence, addition of allylic alkoxide did not bypass the oxidation stage, but addition of alkoxide did increase the yield of **7a** substantially—possibly by formation of an indium "ate" complex. Consistent with this interpretation, reaction of the more conveniently prepared $(C_3H_5)_3In_2Br_3$ (**1**) with **5a** in THF followed by (exothermic) addition of LiBr (or NaOH) and subsequent aerobic workup (addition of Et_2O and then aqueous HCl) afforded **7a** in 82–83 % yield. The formation of an "ate" complex could improve the yield in two distinct ways. First, allylindium "ate" complexes show enhanced reactivity[5c] and selectivity[5d] toward electrophiles relative to their neutral precursors. Second, because rearrangement may compete with hydrolytic cleavage of the In–OC or In–C(4) bonds, the negatively charged "ate" complex may be less susceptible to hydrolysis.


9a: L = I
10a: L = $CH_2{=}CHCH_2O$-


11a

Based on the same procedure—addition of α,β-unsaturated carbonyl compound **5b**, **5c**, **12**, or **13** to allylindium sesquibromide **1** in THF at 25 °C (12 h) followed by formation of the "ate" complex (LiBr, THF, 24 h), dilution with Et_2O, admission of air, and then addition of 1 M HCl—we prepared vinylcyclopropanes **7b** and **7c**, divinylcyclopropane **14**, and spiro-vinylcyclopropane **15** in yields of 79, 52, 92, and 38 %, respectively.

Curiously, α,β-unsaturated ketones and aldehydes have been reported to undergo indium-mediated Barbier-type allylations to afford allylic–homoallylic alcohols **8** in high yield (83–95 %) with no mention of cyclopropane formation (see Scheme 2).[3a, 4b] Indeed, we were able to reproduce reported allylations of **5b** and **5c** to **8b** and **8c** by treatment of allyl iodide with In or InI in THF or DMF and addition at 25 °C of **5b** or **5c** followed by workup after one hour by addition of 1 M HCl. However, we were also able to detect a small amount of cyclopropane **7b** (4 %) in the crude product from reaction of **5b** (→**8b**) by thin-layer chromatography and NMR spectroscopy. Homogeneous acidic conditions (THF/H_3O^+) cause hydrolysis of CO–In and allylic C–In bonds,[4a] in this case converting **6b** and **6c** into **8b** and **8c**. Subsequent addition of Et_2O generates a biphasic mixture, which facilitates separation of the organic products.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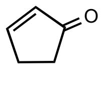
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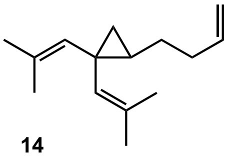
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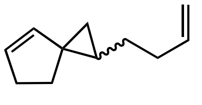
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Somewhat surprisingly, simply inverting the order of addition of aqueous acid and Et_2O (that is, dilution with Et_2O first and then addition of H_3O^+) diverts the reaction pathway of intermediate **6** away from **8** to form **7** instead. The effect of Et_2O addition may be twofold: It reduces the THF concentration and, more important, it results in generation of a biphasic mixture upon addition of the aqueous acid. Intermediate **6**—which bears C(4), C(5), and C(6) prior to transfer—is more soluble in the ethereal phase, and may therefore be protected somewhat from acidic hydrolysis. Acid is essential, however, because under neutral conditions (i.e., addition of water instead of aqueous HCl) no generation of **7** is observed until dilute HCl is introduced.

The intimate details of the mechanism by which **6** is converted into **7** are not obvious. At present we have no evidence as to whether the overall homoallylic to methylenecyclopropane skeletal rearrangement, formation of an allylic C–C bond, and cleavage of the C–OIn bond occurs by covalent, ionic, or radical intermediates. However, the rearrangement does appear to be facilitated by allylic placement of the C–OIn bond, because benzophenone does not lead to a cyclopropane product.

The potential applications of indium-mediated deoxygenative reactions are of considerable scope. Further investigations[9] are underway and will be fully reported in due course.

Experimental Section

7a: Under N_2, allyl bromide (0.530 mL, 6.09 mmol) was added to indium powder (particle size: 100 mesh; Aldrich, 459 mg, 4.00 mmol) in THF (2 mL), which resulted in an exothermic reaction. After 70 min **5a** (235 mg, 1.00 mmol) was added as a solid. After 4 h LiBr (347 mg, 4 mmol) was added (exothermic reaction), and after a further 12 h air was admitted to the reaction vessel. Et_2O (10 mL) and 1M HCl (30 mL) were then introduced, and the biphasic mixture was shaken vigorously at intervals of 10 min over a period of 1 h. The organic phase was separated, dried (Na_2SO_4), and concentrated. Chromatographic purification (silica gel, hexane/EtOAc 19/1) afforded **7a**[6] (249 mg, 83%) as a colorless oil. Elemental analysis calcd for $C_{23}H_{24}$: C 91.95%, H 8.05%; found: C 91.59%, H 8.30%. **7b**, **7c**, **14**, and **15** were prepared similarly. Tenfold scale-up with **5a** afforded **7a** in similar yield.

Keywords: allyl complexes · cyclopropanes · indium · ketones · rearrangements

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[6] $^1H-^1H$ COSY, PECSY, DEPT, $^{13}C-^1H$ COSY (long- and short-range), and 2D-^{13}C INADEQUATE spectra, NOE studies, selective ^1H decoupling, and $^1J_{CC}$ coupling confirmed the structure of **7a**. Complete analytical data for **7b**, **7c**, **14**, and **15** will be reported elsewhere; the diastereomer ratios of **7b**, **7c**, and **15** were 1:1, 2:1, and 4:1. Analyses of the reaction mixtures by thin-layer chromatography indicated no traces of starting materials **5a–c**, **12**, or **13**. Lower yields for **7c** and **15** presumably reflect loss of material through polymerization or formation of highly polar materials.

[7] Compound **5a** reacts with $(C_3H_5)_2In_2I_4$ to give **9a** (and with **1** to give **6a**), as shown by ^1H NMR spectroscopy in $[D_8]$THF. Removal of THF from **9a** under reduced pressure (0.1 Torr), addition and subsequent removal of $PhCH_3$, and dissolution of the residue in $[D_8]$THF resulted in a fluxional ^1H NMR spectrum that revealed no trace of **9a**.

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