



Indium-mediated regioselective allylation of terminal epoxides: a facile synthesis of bishomoallyl alcohols[†]

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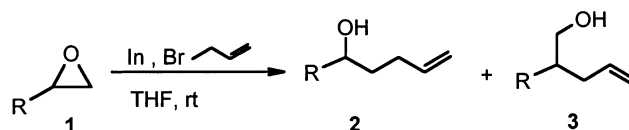
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Abstract—Allyl indium, prepared from allyl bromide and indium metal in THF, reacts with terminal epoxides at room temperature to afford the corresponding bishomoallyl alcohols in excellent yields and with good regioselectivity. © 2001 Elsevier Science Ltd. All rights reserved.

Organometallic compounds have acquired considerable importance in carbon–carbon bond forming reactions.¹ In particular, organoindium reagents have attracted much attention due to their compatibility with many common organic functional groups (e.g. R-OH, CO₂R) and stability under aqueous conditions. Allyl indium reagents,² generated in situ from allyl halides and indium metal, react with various electrophiles, such as carbonyl compounds, C=N unsaturated systems, C–C multiple bonds, acyl halides, aryl halides, and α,β -unsaturated compounds, to generate homoallyl products. Aqueous solvents have proved to be most effective for indium mediated reactions³ and in certain cases significant regio-, diastereo- and even enantioselectivities have been achieved. Epoxides are good electrophiles capable of reacting with organometallic reagents,^{4–6} such as allyl magnesium, allyl zinc, allylsilane, allylstannane and allylcuprate, to generate unsaturated alcohols. However, most of these reagents are expensive, sensitive to both air and moisture, and also some of them require promoters to initiate a reaction. Further, many of these procedures suffer from low regioselectivity, unsatisfactory yields and the formation of side products. The problems associated with these reagents can be overcome by the use of allylindium for this transformation. To the best of our knowledge this is the first report on the allylation of terminal epoxides with indium metal and allylbromide.

In a continuation of our work on the applications of indium for various transformations,⁷ we report here a novel and highly regioselective method for the allylation of terminal epoxides using indium metal and allylbromide in THF. The reaction of styrene oxide with allylindiumbromide at room temperature in THF gave the corresponding products **2** and **3** in 90% yield (Scheme 1).⁸



Scheme 1.

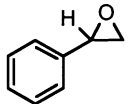
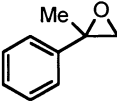
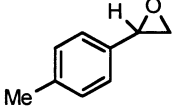
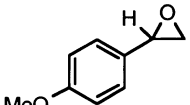
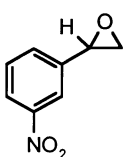
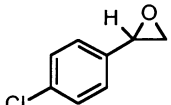
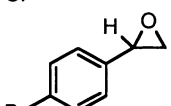
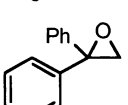
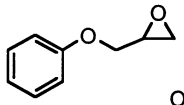
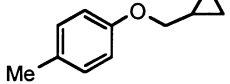
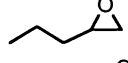
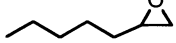
Similarly, several epoxides were treated with allylindium to generate bishomoallyl alcohols in high yields. The reactions proceeded smoothly at room temperature with high regioselectivity. The regioselectivity of this reaction may be explained by the nucleophilic attack on the less hindered carbon atom of the terminal epoxide. The results, as summarized in Table 1, clearly reveal the scope and generality of the reaction with respect to various epoxides. The reactions were clean and highly regioselective, affording the corresponding alcohol **2** with only a trace of the other isomer **3** (Table 1). The epoxides used in this study were prepared by a known literature method. However, the reaction of allylindium with mono-substituted terminal epoxides afforded the product as a mixture of **2** and **3** whereas disubstituted terminal epoxide gave the product as single isomer **2**. The ratio of products **2** and **3** was determined by ¹H NMR spectroscopy and GLC analysis. Further, cyclic epoxides like cyclohexene oxide and

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Table 1. Indium-mediated conversion of epoxides to bishomoallyl alcohols^a

Entry	Epoxide	Reaction Time (h)	Yield ^b (%)	Regioselectivity ^c (2 : 3)
a		3.0	90	90 : 10
b		2.5	95	100 : 0
c		3.0	95	90 : 10
d		3.5	90	100 : 0
e		2.5	90	80 : 20
f		3.5	96	90 : 10
g		3.5	96	90 : 10
h		3.5	96	100 : 0
i		4.0	85	80 : 20
j		4.0	85	80 : 20
k		4.5	80	70 : 30
l		4.5	80	70 : 30

a) All products were characterized by ¹H NMR, IR and Mass spectra.

b) Isolated and unoptimized yields after purification.

c) Ratio of **2** and **3** was determined by ¹H NMR and GLC analysis.

cyclooctene oxide, did not yield any product after a long reaction time at room temperature. The solvent THF is the one of choice, as the best results were obtained. Unlike many zinc- and tin-promoted reactions that use acid catalysts, heat or sonication for inducing the reaction, this reaction proceeds smoothly and rapidly at room temperature and does not require any promoter, stringent conditions, anhydrous solvent or an inert atmosphere. Even though this reaction

proceeded smoothly in commercial THF (containing 0.2% of water), the reaction was unsuccessful in water alone. Among various metals such as Sm, Mg, Zn and Sn studied for this transformation indium is found to be effective in terms of conversion and reaction time.

In summary, we have described a novel and highly efficient protocol for the allylation of terminal epoxides using indium metal and allylbromide in THF. The

procedure offers several advantages including high regioselectivity, improved yields, cleaner reactions, simple experimental and work-up procedures, which make it a useful and attractive strategy for the synthesis of bishomoallylic alcohols.

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- In a typical procedure a suspension of indium powder (5 mmol) and allyl bromide (6 mmol) in 10 ml of THF was stirred until the metal dissolved completely to form a clear solution. To the allyl indium reagent generated as above, a solution of styrene oxide (5 mmol) in THF (5 ml) was added. The resulting reaction mixture was stirred for 3 h at room temperature. After completion of the reaction, as indicated by TLC, the reaction mixture was quenched with saturated ammonium chloride (10 ml) and extracted twice with ether (2×20 ml). The combined organic layers were washed with brine, dried over anhydrous Na₂SO₄, concentrated in vacuo and purified by column chromatography on silica gel (Merck, 60–120 mesh, ethyl acetate:*n*-hexane, 1:9) to afford product in 90% yield as a colorless liquid. Representative spectroscopic data for compound **2a**: ¹H NMR (CDCl₃) δ: 1.80 (brs, OH), 2.25 (m, 2H), 2.75 (m, 2H), 3.80 (m, 1H), 5.15 (m, 2H), 5.80 (m, 1H), 7.25 (m, 5H). IR (neat) ν: 3450, 3150, 2980, 1620, 1580, 1020, 970. **3a**: ¹H NMR (CDCl₃) δ: 2.40 (m, 2H), 2.60 (brs, OH), 2.85 (m, 1H), 3.70 (m, 2H), 5.05 (m, 2H), 5.75 (m, 1H), 7.25 (m, 5H). EIMS (*m/z*): 162 (M⁺).