Pergamon

Tetrahedron Letters 43 (2002) 3333–3335

TETRAHEDRON
LETTERS

# $Yb(OTf)_3$ catalyzed highly regioselective allylation of aromatic epoxides: an efficient route to bishomoallyl alcohols[†]

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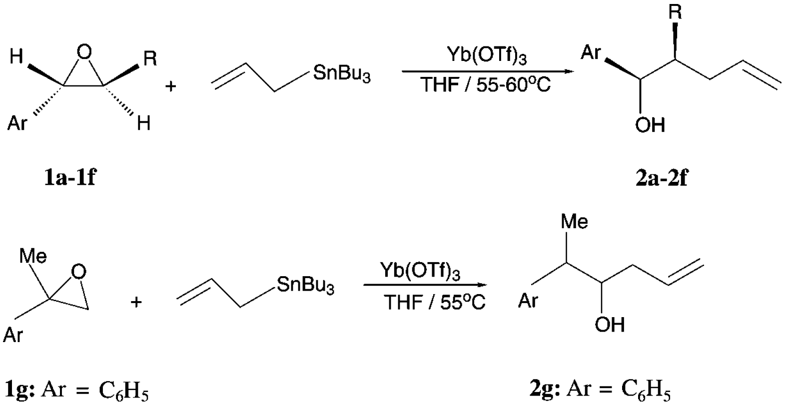
Received 28 August 2001; revised 5 March 2002; accepted 15 March 2002

**Abstract**—Anhydrous ytterbium(III) triflate-catalyzed ring opening of aromatic 1,2-epoxides with allyltributyltin in THF results in the formation of bishomoallyl alcohols in excellent yields and with complete regioselectivity. The results are compared with those obtained with allylmagnesium bromide as allylating agent. © 2002 Elsevier Science Ltd. All rights reserved.

Over the past few years, lanthanide trifluoromethanesulfonates (triflates), $Ln(OTf)_3$, have enjoyed extensive application as catalysts in a variety of Lewis acid activated carbon–carbon bond forming reactions,[1] encompassing Diels–Alder reactions,[2] Michael reactions,[3] Mukaiyama aldol reactions[4] and the allylation of carbonyl compounds.[5] The growing popularity of lanthanide salts in organic synthesis predominantly stems from their putative ease of handling, reusability, robustness towards moisture and air as well as unique reactivity and selectivity. However, despite the exuberant research activities noted above, lanthanide-catalyzed allylation of epoxides, which offers direct access to synthetically useful bishomoallyl alcohols, remains a relatively unexplored area. Furthermore, the reported procedures, which employ various allylmetal reagents,[6,7] are found to have limitations, such as unsatisfactory yields, the non-catalytic nature of the reagent as well as poor chemo- and regioselectivity, thereby restricting their widespread application. Recently, in-situ generated allylindium reagents have also been utilized to achieve syntheses of bishomoallyl alcohols from terminal epoxides, in which both regioisomers are present.[8] Therefore, a totally regiocontrolled procedure for the ring opening of oxiranes by allyl transfer agents is highly demanding. Herein, we report, as a part of our continuing effort to explore the novel reactivity of lanthanide catalysts,[9,10] our results in the $Yb(OTf)_3$-cat-



**Scheme 1.** **a**: $Ar=C_6H_5$, $R=H$; **b**: $Ar=C_6H_5$, $R=C_6H_5$; **c**: $Ar=2Br\text{-}C_6H_4$, $R=H$; **d**: $Ar=3Cl\text{-}C_6H_4$, $R=H$; **e**: $Ar\text{-}4Me\text{-}C_6H_4$, $R=H$; **f**: $Ar=4\text{-benzyloxy-3-nitro-}C_6H_3$, $R=H$.

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*Keywords*: ytterbium triflate; allylation; epoxide ring opening; allyltributyltin; unsaturated alcohol.

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[†] Dedicated to Professor Thomas P. Fehlner on the occasion of his 65th birthday. This is IICT Communication No. 4832.

PII: S0040-4039(02)00522-1

alyzed allylation of aromatic 1,2-epoxides with allyltributyltin, providing a facile route to bishomoallyl alcohols.

The reactions of **1a**–**1f** with allyltributyltin proceed smoothly under the catalytic influence of $Yb(OTf)_3$ (15 mol% with respect to the epoxide) in THF with nearly quantitative conversion resulting in the formation of the corresponding unsaturated alcohols **2a**–**2f** as predominantly one regioisomer (Scheme 1).[11] The experimental results, compiled in Table 1, amply demonstrate the generality of the reaction with regard to substitution in the aromatic ring. Thus, substitution either at the *ortho*, *meta* or *para* position does not seem to show any appreciable effect on the conversion and selectivity (entry 1 versus entries 2–6). Also, substrates containing electron donating groups **1c**–**1e** (entries 3–5) and that containing an electron withdrawing group **1f** (entry 6) exhibited similar reactivity patterns, thus implying that the electronic nature of the substituent does not have any noticeable influence on the reaction. Strikingly, in most of the occasions, except **2a** and **2f** (where minor products were observed in the NMR spectra), single regioisomers, resulting from nucleophilic attack exclusively at the less substituted carbon (for terminal epoxides), are obtained. In the case of the 1,1-disubstituted epoxide **1g** (entry 7) the product alcohol **2g** resulted from $Yb(OTf)_3$ induced rearrangement of the epoxide[12] followed by allylation at the less substituted carbon (Scheme 1). It is noteworthy that the products **2b** and **2g** are obtained as single diastereoisomers, as determined by $^1H$ NMR.[11] The total diastereoselectivity may appear to be indicative of an associative mechanism, which is expected to give rise to the *erythro* isomer exclusively.[10] Cyclic epoxides such as cyclohexene oxide, cyclooctene oxide or norbornene oxide as well as aliphatic open chain epoxides namely 2,3,3-trimethyl-1-butene oxide, 2,3-dimethyl-2-butene oxide, 1,3-dichloropropane oxide did not yield any product after long reaction times at elevated temperatures.

**Table 1.** $Yb(OTf)_3$-catalyzed conversions of epoxides using allyltributyltin to give homoallyl alcohols[a]

| Entry | Substrate | Time (h)/temp. (°C) | Product[b] | Yield[c] (%) |
|---|---|---|---|---|
| 1 | **1a** | 25/55 | **2a** | 97 |
| 2 | **1b** | 22/60 | **2b** | 96 |
| 3 | **1c** | 20/55 | **2c** | (94) |
| 4 | **1d** | 20/55 | **2d** | 98 |
| 5 | **1e** | 21/55 | **2e** | (95) |
| 6 | **1f** | 22/60 | **2f** | 98 |
| 7 | **1g** | 20/55 | **2g** | (92) |
| 8[d] | **1a** | 25/60 | **2a** | 40 |

[a] Reaction conditions: epoxide (0.5 mmol), allyltributyltin (0.55 mmol), $Yb(OTf)_3$ (0.075 mmol), THF (4 ml).[11]

[b] Products characterized either on the basis of spectroscopic data reported elsewhere[7,12a,13] or reported here.[11]

[c] Isolated yield based on the epoxide used, values in parentheses refer to GLC yield.[14]

[d] Catalyst, recycled after single use, is employed.[15]

**Table 2.** Lanthanide triflate-catalyzed reactions of styrene oxide **1a** with allyltributyltin[a]

| Entry | Catalyst | Time (h)/temp. (°C) | Yield of **2a** (%) |
|---|---|---|---|
| 1 | $Sc(OTf)_3$ | 21/60 | 96 |
| 2 | $Yb(OTf)_3$ | 21/60 | 91 |
| 3 | $Y(OTf)_3$ | 21/60 | 77 |

[a] Reaction conditions: epoxide (0.5 mmol), allyltributyltin (0.55 mmol), catalyst (0.075 mmol), THF (4 ml).

**Table 3.** $Yb(OTf)_3$-catalyzed reactions of epoxides with (allyl)MgBr[a]

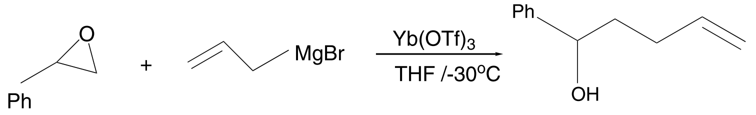
| Entry | Substrate | Time (h)/temp. (°C) | Product | Yield[b] (%) |
|---|---|---|---|---|
| 1 | **1a** | 1/−40 | **2a** | 71 (79) |
| 2 | **1b** | 1/0 | **2b** | 41 (46) |
| 3 | **1c** | 7/rt | **2c** | 55 (59) |
| 4 | **1e** | 3/0 | **2e** | 42 (48) |
| 5 | **1g** | 7/rt | **2g** | 54 (56) |

[a] Reaction conditions: epoxide (0.5 mmol), (allyl)MgBr (1.5 mmol), $Yb(OTf)_3$ (0.075 mmol), THF (4 ml).[16]

[b] Isolated yield. Values in parentheses refer to GLC yield.

Among the various metal triflates employed as catalysts, namely $Sc(OTf)_3$, $Y(OTf)_3$ and $Yb(OTf)_3$, the last one is the best suited for this reaction considering that it is the least expensive, easy to prepare and yet has a high catalytic activity (Table 2). The reusability of $Yb(OTf)_3$ was tested by exposing the catalyst, isolated from the reaction mixture (entry 1, Table 1),[15] to a fresh batch of **1a** under identical reaction conditions (entry 8, Table 1) with **2a** being formed in 40% isolated yield. The low yield may be partly attributed to the loss of the catalyst complex and/or absorption of moisture during the isolation procedure.

We also examined the reactivity of allylmagnesium bromide as the allylating reagent (Scheme 2).[16] In all occasions, the optimized product yields are substantially lower (Table 3) compared with those obtained using



**1a** **2a**

**Scheme 2.**

(allyl)SnBu$_3$, however, the reaction proceeds with the same regioselectivity as depicted in Scheme 1.

In summary, a simple, highly efficient method for the preparation of bishomoallylic alcohols from aromatic 1,2-epoxides is presented, which utilizes Yb(OTf)$_3$ to achieve a totally regioselective ring opening.

## Acknowledgements

The authors are grateful to the Department of Science and Technology, New Delhi (Grant No.SP/S1/F11/97) and the Director IICT for financial support (MLP-2711). Valuable comments from the Referee are thankfully acknowledged.

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11. In a typical run, the epoxide (0.5 mmol) and allyltributyltin (0.55 mmol) were added to a stirred solution of anhydrous ytterbium triflate (0.075 mmol, 15 mol%) in dry and freshly distilled THF (4 ml). The stirring was continued at the reaction temperature for the required period of time (monitored by TLC). On completion, the reaction mixture was diluted with water (5 ml) and the aqueous layer was washed with dichloromethane (3×5 ml). The combined organic extract was dried over anhydrous sodium sulfate. Partial evaporation of the solvent followed by separation on a silica gel column (1.5×7 cm, 60–120 mesh, petroleum ether/ethyl acetate 97/3 as eluent) afforded analytically pure bishomoallyl alcohol as a single isomer. The isolated yield was calculated based on the amount of epoxide used and 98–99% mass balance was obtained. The products were characterized using $^1$H NMR, IR and mass spectroscopy. Representative spectroscopic data for compound **2a** (liquid): $^1$H NMR (CDCl$_3$) $\delta$: 2.05–2.35 (m, 2H), 2.70 (m, 2H), 3.75 (m, 1H), 5.01–5.1 (m, 2H), 5.80 (m, 1H), 7.1–7.3 (m, 5H); EI MS $m/z$: 162. **2b** (liquid): $^1$H NMR (CDCl$_3$) $\delta$: 2.02–2.39 (m, 2H), 3.9 (d, 1H, $J=9.4$ Hz), 4.25–4.45 (m, 1H), 4.99 (s, 1H), 5.1 (d, 1H, $J=7.1$ Hz), 5.8–6.0 (m, 1H), 7.1–7.4 (m, 10H); EI MS $m/z$: 238. **2f** (liquid): $^1$H NMR (CDCl$_3$) $\delta$: 2.05–2.38 (m, 2H), 2.6–2.85 (m, 2H), 3.75–3.9 (m, 1H), 5.05–5.25 (m, 4H), 5.7–5.9 (m, 1H), 7.0 (d, 1H, $J=10$ Hz), 7.27–7.45 (m, 6H), 7.7 (d, 1H, $J=2.5$ Hz); EI MS $m/z$: 313. **2g** (liquid): $^1$H NMR (CDCl$_3$) $\delta$: 1.2–1.3 (d, 3H), 1.85–2.2 (m, 2H), 2.7 (m, 1H), 3.55 (m, 1H), 4.95 (s, 1H), 5.05 (d, 1H, $J=10$ Hz), 5.6–5.9 (m, 1H), 7.06–7.32 (m, 5H). EI MS $m/z$: 177.
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14. Shimadzu GC-14B equipped with flame ionization detector and SE-30 packed column.
15. Yb(OTf)$_3$ catalyst was recovered from the reaction mixture (cf. entry 1, Table 1) by following the procedure described in Refs. 9, 10.
16. Epoxide (0.5 mmol) and (allyl)MgBr (1.5 mmol) were added to a stirred solution of Yb(OTf)$_3$ (0.075 mmol, 15 mol%) in dry, freshly distilled THF (4 ml) at −30°C. The stirring was continued at the reaction temperature for the requisite time (monitored by TLC). The reaction was quenched by adding saturated aq. NH$_4$Cl solution, the aqueous layer was extracted with diethyl ether (3×5 ml) and the product was isolated as described above (cf. Ref. 11).