# Bismuth Triflate Catalyzed [1,3] Rearrangement of Aryl 3-Methylbut-2-enyl Ethers

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**Abstract:** An efficient bismuth triflate catalyzed [1,3] rearrangement of aryl 3-methylbut-2-enyl ethers has been developed. The reaction proceeds rapidly and affords the corresponding *para*- and *ortho*-prenylated phenols and naphthols in moderate to good yields (up to 86%). *ortho*-Prenylphenols are immediately cyclized under the reaction conditions to the corresponding chroman derivatives.

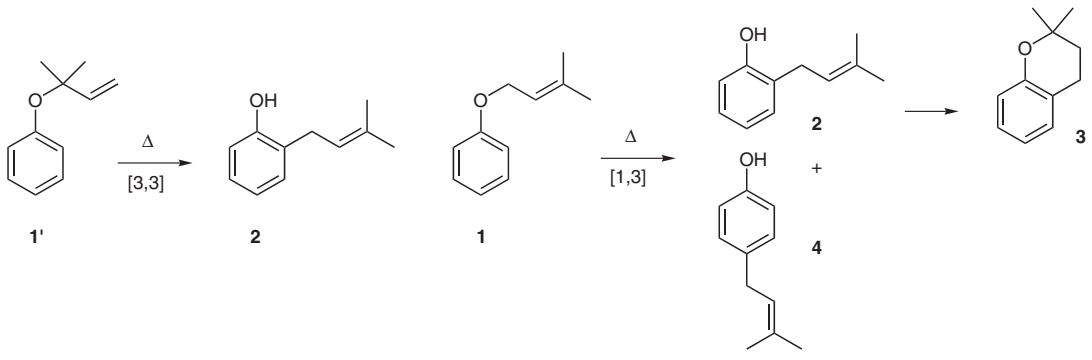
**Key words:** bismuth, bismuth triflate, [1,3] rearrangement, Lewis acid, allyl phenyl ethers

The [3,3] sigmatropic shift (Claisen rearrangement) of allyl aryl ethers provides a convenient access to *ortho*-allyl phenols and naphthols,[1] which are versatile intermediates in the synthesis of biologically active compounds such as 1,4-naphthoquinones and anthracyclinones.[2] The difficulty in preparing 2,2-disubstituted ethers such as **1′** renders the Claisen rearrangement inconvenient for the preparation of terminally substituted *ortho*-allylphenols **2**. A mild and convenient method for the [1,3] rearrangement of ether **1** is therefore desirable as an alternative to the Claisen rearrangement (Equation 1).

Although the [1,3] rearrangement provides an efficient synthetic route for the preparation of *ortho*- or *para*-prenylated phenols along with chroman derivatives **3**, it usually requires high temperatures to proceed.[3] These forcing conditions lead to severe side reactions. Recently, synthetic methods involving Al(III) derivatives, lanthanide triflates, and clays as catalysts for the [1,3] sigmatropic rearrangement of allyl aryl ethers have been reported.[4] Bismuth compounds have attracted recent attention due to their low toxicity, low cost, and good stability.[5] Bismuth salts have been reported as catalysts for opening of epoxides,[6] Mukaiyama aldol and Mannich-type reactions,[7] formation of acetals,[8] Sakurai reactions,[9] Friedel–Crafts reactions and Fries rearrangements.[10] $Bi(OTf)_3$ is particularly attractive because it is commercially available or can be easily prepared from readily available starting materials.[11]

We recently reported the bismuth(III)-catalyzed [3,3] rearrangement (Claisen rearrangement) of allyl 1-naphthyl ethers.[12] When a crotyl 1-naphthyl ether was used, a mixture of [3,3] and [1,3] products was obtained, with the expected Claisen rearrangement being the major pathway. The general effectiveness of $Bi(OTf)_3$ as a Lewis acid brought us to study the desired [1,3] shift. We found that [1,3] rearrangement of substituted 3-methylbut-2-enyl naphthyl ethers was efficiently catalyzed by $Bi(OTf)_3 \cdot 4H_2O$ in mild conditions. Both *ortho*- and *para*-prenylated naphthols and phenols are readily obtained in the presence of 5 mol% of $Bi(OTf)_3$. Among various catalyst loadings tested, 5 mol% of $Bi(OTf)_3$ was found to give the rearranged products with the best yield. Under our conditions, the corresponding Claisen [3,3] rearrangement was never observed.

Initially, we screened the [1,3] rearrangement on differently 2- and 4-substituted allyl 1-naphthyl ethers (Table 1). The substituted 1-naphthyl prenyl ethers **5a–d** were first prepared according to the usual procedure (pre-




**Equation 1**

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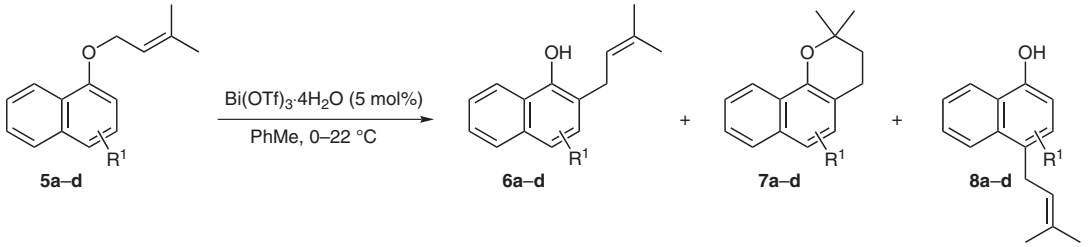



**Scheme 1**

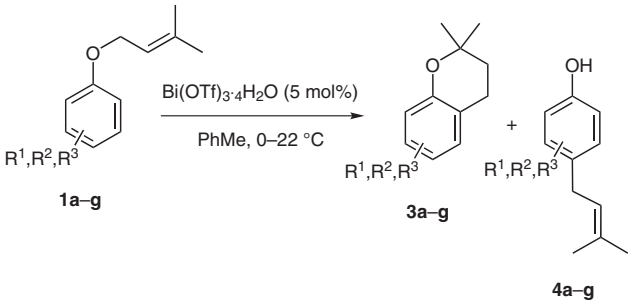
nyl bromide, $Cs_2CO_3$, DMF, 22 °C). The rearrangement occurs with 5 mol% $Bi(OTf)_3{\cdot}4H_2O$ in an apolar solvent such as toluene (Scheme 1). The *ortho*- and *para*-substituted naphthol derivatives **6** and **8**, along with the corresponding chroman derivatives **7** were isolated in moderate to good yields. 1-Naphthyl prenyl ether **5a** afforded *ortho*-prenylnaphthol (**6a**) in a moderate yield (72%) (Table 1, entry **a**). Whatever the substitution of the naphthol ring, the reaction occurred smoothly to give the corresponding *ortho*- or *para*-prenylnaphthols **6** or **8** (Table 1, entries **a**–**c**). With *ortho*-substituted 1-naphthyl prenyl ethers, the [1,3] rearrangement afforded the corresponding *para*-prenylnaphthols **8b** (Table 1, entry **b**). 1-(3-Methylbut-2-enyloxy)-4-methoxynaphthalene (**5c**) was smoothly rearranged into the *ortho* isomer **6c** (Table 1, entry **c**). The transfer of the allyl group in a [1,3] fashion was also effective with the 4-chloronaphthyl prenyl ether and was immediately followed by a cyclization reaction affording **7d** in a good yield (Table 1, entry **d**). Such a sequential reaction involving a [1,3] rearrangement and a cationic cyclization reaction has already been reported in a clay-catalyzed rearrangement.[4d,e]

From thereon, we further studied the scope and limitations of this reaction with differently substituted 3-methylbut-2-enyl phenyl ethers **1** (Scheme 2). The corresponding *para*-prenylphenols **4** were obtained in moderate to good yield with 5 mol% of $Bi(OTf)_3{\cdot}4H_2O$ in toluene (Table 2, entries **a**, **b**, and **g**). With *para*-substituted substrates, the [1,3] rearrangement immediately followed by a subsequent cationic cyclization occurred in moderate to good yields to give chroman derivatives **3** (Table 2, entries **c**–**f**). The rearrangement occurred in the presence of either an ester or a ketone functionality (Table 2, entries **f** and **g**).

**Table 1** $Bi(OTf)_3$-Catalyzed [1,3] Rearrangement of 3-Methylbut-2-enyl 1-Naphthyl Ethers **5**

| Entry | $R^1$ | Time (h)[a] | Yield **6** (%)[b] | Yield **7** (%)[b] | Yield **8** (%)[b] |
|---|---|---|---|---|---|
| **a** | H | 4.5 | 72 (**6a**) | – | – |
| **b** | 2-COMe | 10 | – | – | 52 (**8b**) |
| **c** | 4-OMe | 19 | 86 (**6c**) | – | – |
| **d** | 4-Cl | 23 | – | 80 (**7d**) | – |

[a] Conditions: 5 mol% $Bi(OTf)_3{\cdot}4H_2O$, PhMe, 0 °C, 2 h, then 22 °C, 2.5–21 h.
[b] Isolated yield.




**Scheme 2**

It is likely that the reaction conditions promote formation of a discrete, delocalized prenyl carbocation and bismuth aryloxide, which recombine to give the desired product. Detailed investigations on the mechanism of this transformation are in progress.

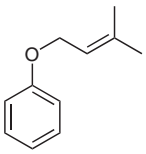
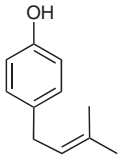
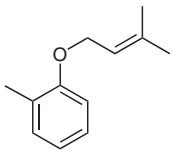
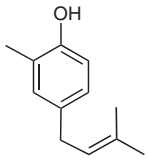
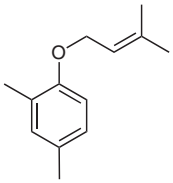
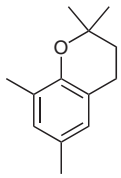
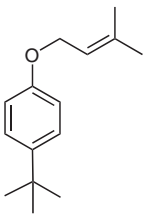
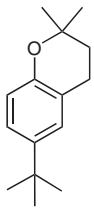
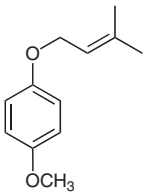
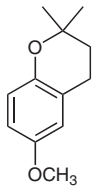
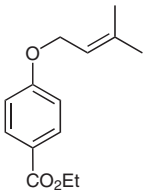
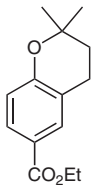
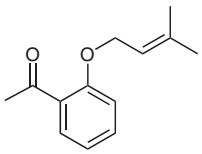
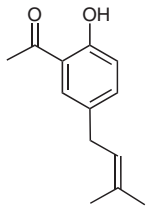
In summary, we have found that $Bi(OTf)_3{\cdot}4H_2O$ is an efficient catalyst for the [1,3] rearrangement of aryl prenyl ethers. The method offers several advantages including mild reaction conditions, use of an environmentally benign catalyst, and no formation of by-products.

$^1$H NMR spectra were recorded on a 400 MHz (100 MHz for $^{13}$C NMR) magnetic resonance spectrometer in $CDCl_3$. Column chromatography was performed on silica gel (230–400 mesh) and analytical TLC was carried out using 250 μm commercial silica gel plates. All glassware was stored in the oven and flame-dried prior to use under an inert atmosphere of argon. Toluene was distilled from sodium. Aryl 3-methylbut-2-enyl ethers **1** and **5** were synthesized according to known literature procedures.[13]

**Bismuth Triflate-Catalyzed [1,3] Rearrangement of Aryl 3-Methylbut-2-enyl Ethers 1 and 5; General Procedure**

To a solution of aryl 3-methylbut-2-enyl ether **1** or **5** (1 mmol) in toluene (10 mL) at 0 °C was added $Bi(OTf)_3{\cdot}4H_2O$ (0.05 mmol). The mixture was magnetically stirred at 0 °C for 2 h, allowed to reach r.t., and then stirred at this temperature for 2.5–21 h. After addition of $H_2O$, the mixture was extracted with EtOAc, washed with $H_2O$, dried ($Na_2SO_4$), filtered, and concentrated under vacuum (rotatory evaporator). The residue was purified by column chromatography on silica gel using hexanes–EtOAc (93:7–90:10) as eluent. Products **3e**,[14a] **3f**,[14b] **3g**,[14c] **4a**,[4e] **4b**,[14d] **4e**,[4d] **4g**,[14e] **6a**,[14f] **7d**,[12] and **8b**[14g] accord exactly with those previously reported in the literature.

**Table 2** Bi(OTf)$_3$-Catalyzed [1,3] Rearrangement of Various Substituted 3-Methylbut-2-enyl 1-Phenyl Ethers **1**

| Entry | **1** | Time (h)[a] | Major product | Yield **3** (%)[b] | Yield **4** (%)[b] |
|---|---|---|---|---|---|
| **a** |  | 12 |  | – | 64 (**4a**) |
| **b** |  | 17 |  | – | 65 (**4b**) |
| **c** |  | 18 |  | 80 (**3c**) | – |
| **d** |  | 14 |  | 78 (**3d**) | – |
| **e** |  | 12 |  | 76 (**3e**) | 3 (**4e**) |
| **f** |  | 16 |  | 80 (**3f**) | – |
| **g** |  | 14 |  | 11 (**3g**) | 68 (**4g**) |

[a] Conditions: 5 mol% Bi(OTf)$_3$·4H$_2$O, PhMe, 0 °C, 2 h, then 22 °C, 10–16 h.
[b] Isolated yield.

**4-Methoxy-2-(3-methylbut-2-enyl)naphthalen-1-ol (6c)**
Yield: 86%.

IR (film): 3381, 3069, 2974, 2934, 2854, 1661, 1596, 1450, 1378 cm$^{-1}$.

$^1$H NMR (400 MHz, CDCl$_3$): δ = 8.13 (d, *J* = 8.3 Hz, 1 H), 8.05 (d, *J* = 8.4 Hz, 1 H), 7.53 (m, 1 H), 7.45 (m, 1 H), 6.64 (s, 1 H), 5.30 (m, 2H), 3.90 (s, 3 H), 3.50 (d, *J* = 7.2 Hz, 2 H), 1.78 (s, 3 H), 1.76 (s, 3 H).

$^{13}$C NMR (100 MHz, CDCl$_3$): δ = 147.9, 147.0, 133.1, 130.1, 129.0, 126.7, 124.9, 124.3, 123.0, 122.1, 110.3, 62.3, 28.4, 26.0, 18.2.

Anal. Calcd for C$_{16}$H$_{18}$O$_2$: C, 79.31; H, 7.49; O, 13.21. Found: C, 78.93; H, 7.69; O, 12.87.

**2,2,6,8-Tetramethylchroman (3c)**
Yield: 80%.

IR (film): 3004, 2975, 2925, 2852, 1481, 1449, 1382, 1368 $cm^{-1}$.

$^1H$ NMR (400 MHz, $CDCl_3$): δ = 6.80 (s, 1 H), 6.74 (s, 1 H), 2.72 (t, *J* = 6.8 Hz, 2 H), 2.24 (s, 3 H), 2.15 (s, 3 H), 1.78 (t, *J* = 6.8 Hz, 2 H), 1.33 (s, 6 H).

$^{13}C$ NMR (100 MHz, $CDCl_3$): δ = 150.2, 129.4, 128.1, 126.3, 120.2, 73.9, 33.4, 33.2, 27.3, 22.9, 20.8, 20.7, 6.3.

Anal. Calcd for $C_{13}H_{18}O$: C, 82.06; H, 9.53; O, 8.41. Found: C, 81.70; H, 9.72; O, 8.04.

**6-*tert*-2,2-Dimethylchroman (3d)**
Yield: 78%.

IR (film): 2963, 2869, 1498, 1481, 1462 $cm^{-1}$.

$^1H$ NMR (400 MHz, $CDCl_3$): δ = 7.10 (d, *J* = 8.6 Hz, 1 H), 7.03 (s, 1 H), 6.69 (d, *J* = 8.6 Hz, 1 H), 2.77 (t, *J* = 6.8 Hz, 2 H), 1.78 (t, *J* = 6.8 Hz, 2 H), 1.20–1.30 (m, 15 H).

$^{13}C$ NMR (100 MHz, $CDCl_3$): δ = 151.9, 142.4, 126.4, 124.6, 120.2, 116.8, 74.2, 34.2, 33.2, 31.9, 27.5, 23.2.

Anal. Calcd for $C_{15}H_{22}O$: C, 82.52; H, 10.16; O, 7.33. Found: C, 82.25; H, 10.50; O, 6.98.

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