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# 1,*n*-Rearrangement of Allylic Alcohols Promoted by Hot Water: Application to the Synthesis of Navenone B, a Polyene Natural Product

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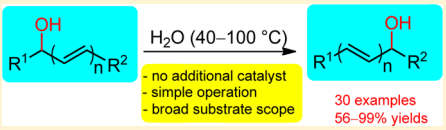
Supporting Information

**ABSTRACT:** It was reported for the first time that hot water as a mildly acidic catalyst efficiently promoted 1,*n*-rearrangement (*n* = 3, 5, 7, 9) of allylic alcohols. In some cases, the rearrangement reactions joined isolated C−C double or triple bonds to generate conjugated polyene or enyne structure motifs. We used the 1,3-rearrangement reaction of an allylic alcohol in hot water as part of an attractive new strategy for construction of the polyene natural product navenone B by iterative use of a Grignard reaction, a 1,3-rearrangement of the resulting allylic alcohol, and subsequent oxidation of the rearranged product.




## INTRODUCTION

Rearrangement reactions are useful for the preparation of synthetically challenging products from readily accessible precursors. The two regioisomers of an asymmetrically substituted allylic alcohol generally have different thermodynamic stabilities as a result of differences in the extent of conjugation or substitution. If the less synthetically accessible isomer happens to be the more thermodynamically stable one, it can be readily obtained through a 1,3-rearrangement reaction of the more synthetically accessible isomer. Furthermore, if the carbon atom bearing the hydroxyl group is substituted with an additional C−C double bond or a triple bond, the 1,3-rearrangement reaction can bring the isolated unsaturated bonds together to form a system with extended conjugation (Scheme 1a). Therefore, these rearrangement reactions may play important roles in the construction of conjugated polyenes and enynes, which are common structural motifs in a great variety of natural products, including retinoids, rapamycin, amphotericin B, cicutoxin, and fumagillin.[1,2]

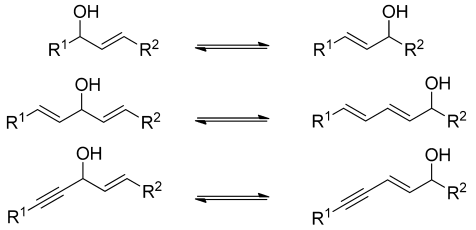
Some catalysts, including Brønsted acids,[3] Lewis acids,[4] transition metal complexes,[5] and transition metal oxo complexes,[6] can mediate 1,3-rearrangement of allylic alcohols. In addition to 1,3-rearrangements of allylic alcohols, 1,*n*-rearrangements (*n* = 5, 7, 9) of conjugated polyenols was synthetically useful and can also generate polyenes with extended conjugation. However, most of the literature reports have focused on 1,3-rearrangements, and 1,*n*-rearrangements (*n* = 5, 7, 9) of conjugated polyenols (Scheme 1b) have rarely been studied,[7] perhaps because conjugated polyenols are readily oxidized and undergo polymerization or cycloaddition reactions. Thus, it is highly desirable to develop an efficient and widely applicable method for 1,*n*-rearrangements of allylic alcohols.

Water, the most abundant liquid on the Earth and solvent in which most of the chemistry of biological processes occurs, is cheaper, safer, and cleaner than organic solvents. In addition to being a green reaction medium, it has unique chemical and physical properties that allow it to catalyze organic reactions.[8] One particularly striking example, reported by Jamison and coworkers, is a water-promoted cascade epoxide-opening via 6-endo mode, yielding a *trans*-fused ladder-type polyether (Scheme 2).[8i] This finding suggests that water might catalyze the biosynthesis of ladder-type polyether natural products.

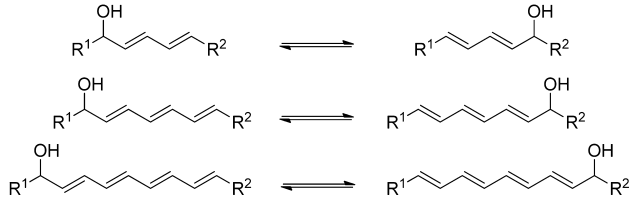
Water is only weakly self-ionizing at 25 °C (p$K_w$ = 14).[9] However, as temperature is increased, the extent of self-ionization increases substantially; the p$K_w$ of water reaches its highest value (11.2) at 250 °C, at which both the strong acid $H_3O^+$ and the strong base $OH^-$ are more abundant than that at

**Scheme 1. Rearrangements of Allylic Alcohols**

a) 1,3-rearrangement of allylic alcohols




b) 1,5-, 1,7- and 1,9-rearrangement of allylic alcohols

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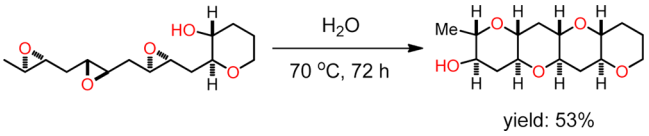
**Scheme 2. Epoxide-Opening Cascades Promoted by Water**



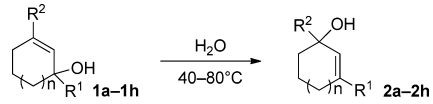

25 °C.[9] Increasing the temperature also decreases the dielectric constant of water, making it a better solvent for organic compounds. Studies of organic reactions in high-temperature or near-critical water (200−374 °C) have shown that organic reactions traditionally catalyzed by Brønsted acids can take place in high-temperature water in the absence of an additional catalyst, and extensive mechanistic studies have suggested that at high temperature, water acts as a mildly acidic catalyst in these reactions.[10] Unlike high-temperature water under pressure, hot water (60−100 °C) is more accessible both in the laboratory and in nature. In previous studies, we found that hot water can act as a mildly acidic catalyst, which is similar to high-temperature water.[11] Recently, we found that the $S_N1$ hydrolysis of allylic and benzylic alcohols occurs in hot water, and we systematically studied the effects of various reaction parameters on the outcome of this reaction.[11d] Our findings inspired us to explore further the applications of hot water chemistry to organic synthesis. Herein, we report that hot water efficiently promoted 1,*n*-rearrangements of allylic alcohols, in many cases forming conjugated polyenes or enynes that would be difficult to synthesize by other means. We also describe the iterative use of a Grignard reaction of an aldehyde, a 1,3-rearrangement of the resulting allylic alcohol in hot water, and subsequent oxidation of the rearranged allylic alcohol to efficiently construct a conjugated polyene natural product via a modular approach.

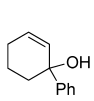
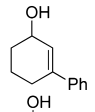
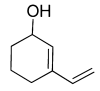
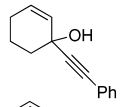
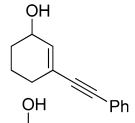
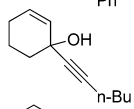
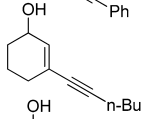
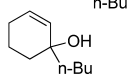
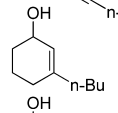
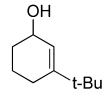
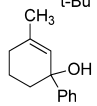
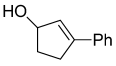
## RESULTS AND DISCUSSION

We began with investigating whether the 1,3-rearrangement of 1-phenyl-2-cyclohexen-1-ol (**1a**) occurred in water in the absence of an additional catalyst. We found that no reaction occurred when **1a** was heated in an aprotic organic solvent such as THF, 1,4-dioxane, toluene, acetonitrile, or DMF or in a protic organic solvent such as methanol or isopropanol, even after prolonged reaction times. However, at 80 °C in water, the reaction was complete after 9 h and afforded the thermodynamically more stable isomer **2a** almost quantitatively (1 mmol of **1a** did not dissolve completely in 25 mL of water; the reaction mixture was a slightly hazy solution even at 80 °C). The fact that **1a** remained inert in methanol or isopropanol at their refluxing temperature indicated that the rearrangement did not initiate at raised temperature in a polar solvent that is capable of forming hydrogen bond and confirmed that water played a catalytic role in the reaction.

We then carried out 1,3-rearrangements of various other cyclic allylic alcohols in hot water (Table 1). Reactions of **1a**−**1f**, which have six-membered rings bearing various phenyl, vinyl, alkynyl, and alkyl groups, afforded good to excellent yields of products **2a**−**2f** (entries 1−6), and some of them are conjugated diene or enyne (**2b**−**2d**). It is noteworthy that even at 80 °C, allylic alcohol **1g** gave the desired rearrangement product (**2g**) in 93% yield and none of the elimination product (entry 7). Five-membered-ring allylic alcohol **1h** gave a 90% yield of **2h** after 0.5 h at 40 °C (entry 8). We attributed the high activity of these cyclic allylic alcohols to the effects of

**Table 1. Hot Water-Promoted 1,3-Rearrangements of Cyclic Allylic Alcohols**[a]




| entry | substrate | temp (°C) | time (h) | product | yield (%)[b] |
|---|---|---|---|---|---|
| 1 | **1a**  | 80 | 12 | **2a**  | 96 |
| 2 | **1b**  | 80 | 12 | **2b**  | 95 |
| 3 | **1c**  | 80 | 16 | **2c**  | 91 |
| 4 | **1d**  | 80 | 14 | **2d**  | 86 |
| 5 | **1e**  | 80 | 12 | **2e**  | 91 |
| 6 | **1f**  | 80 | 30 | **2f**  | 83 |
| 7 | **1g**  | 80 | 6 | **2g**  | 93 |
| 8 | **1h**  | 40 | 0.5 | **2h**  | 90 |

[a]Reaction conditions: 1 mmol of allylic alcohol in water (25 mL), vigorously stirring. [b]Isolated yield.

"allylic strain",[12] which favors the production of less-strained, more thermodynamically stable isomers.

Compared to cyclic allylic alcohols, acyclic allylic alcohol **1i** underwent the 1,3-rearrangement very slowly in water even when the temperature was raised to 100 °C (Table 2, entries 1, 2). However, to our delight, the reaction was markedly accelerated when a small amount of organic solvent was introduced to disperse the substrate, and the effect of 1,4-dioxane was more pronounced than that of THF (Table 1, entries 3, 8). The addition of 10 vol % 1,4-dioxane considerably sped up the reaction by improving the solubility of organic reactant in the aqueous solution (entry 9). The more effectiveness of water/1,4-dioxane mixed solvent than water/THF mixed solvent may be due to the higher boiling point of water/1,4-dioxane binary system. However, when the volume percentage of the organic solvent was further increased, the reaction rate decreased drastically (entries 4−7, 10−13). It may be partly because of a reduction in the extent of ionization of water,[13] a decrease in the dielectric constant, or both.

The reactions of acyclic allylic alcohol substrates were explored under the optimal conditions (Table 3). Phenyl-, naphthyl-, and thienyl-substituted substrates **1i**−**1l** (entries 1−4) all gave the desired products with *E* selectivity. Notably, **1j**, which has an acid-sensitive phenolic silyl group, tolerated the reaction conditions (entry 2). Tertiary substituted alcohols **1m** and **1n** afforded allylic alcohols with trisubstituted alkene moieties (entries 5, 6). Substrates **1o**−**1r** with alkyl substituents


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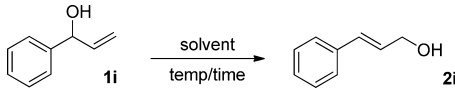
**Table 2. Effects of Solvent and Temperature on the 1,3-Rearrangement of Allylic Alcohol 1i[a]**



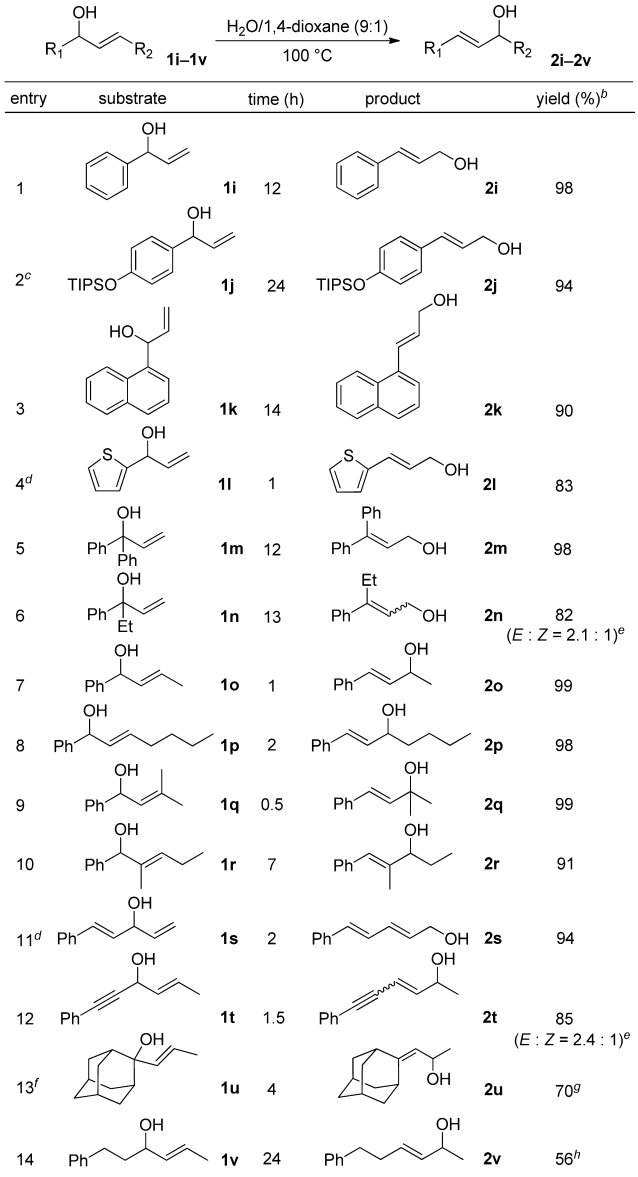

| entry | solvent | temp (°C) | time (h) | yield/conv (%)[b] |
|---|---|---|---|---|
| 1 | $H_2O$ | 80 | 48 | 2/5 |
| 2 | $H_2O$ | 100 | 48 | 7/10 |
| 3 | $H_2O$:THF = 9:1 | 80 | 48 | 18/24 |
| 4 | $H_2O$:THF = 4:1 | 80 | 48 | 7/10 |
| 5 | $H_2O$:THF = 1:1 | 80 | 48 | NR |
| 6 | $H_2O$:THF = 1:4 | 80 | 48 | NR |
| 7 | $H_2O$:THF = 1:9 | 80 | 48 | NR |
| 8 | $H_2O$:1,4-dioxane = 9:1 | 80 | 48 | 78/96 |
| 9 | $H_2O$:1,4-dioxane = 9:1 | 100 | 12 | 98/100 |
| 10 | $H_2O$:1,4-dioxane = 4:1 | 100 | 16 | 96/100 |
| 11 | $H_2O$:1,4-dioxane = 1:1 | 100 | 48 | 43/64 |
| 12 | $H_2O$:1,4-dioxane = 1:4 | 100 | 48 | NR |
| 13 | $H_2O$:1,4-dioxane = 1:9 | 100 | 48 | NR |

[a]Reaction conditions: 1 mmol of **1i** in solvent (25 mL), vigorously stirring. [b]Isolated yield.

on alkene afforded very high yields of products **2o**−**2r** (entries 7−10). Allylic alcohols **1s** and **1t**, which are substituted with styryl and phenylethynyl groups, respectively, reacted smoothly to afford diene **2s** and enyne **2t** in high yield (entries 11, 12). The hydroxy group of **1s** could have rearranged either to the benzylic position or to the end of the alkyl chain, but only diene **2s**, which has more-extended conjugation, was formed (entry 11). When the reaction of adamantyl-substituted allylic alcohol **1u** reached equilibrium after 4 h, we obtained about 70% of isomer **2u**, which is less sterically congested and has a more highly substituted olefin bond. In the meantime, 23% of isomer **2u** was transformed to the *Z*-configuration isomer **1u** (entry 13). Secondary alcohol substrates with an aliphatic side chain are unreactive in the presence of polyfluorinated arylboronic acids in toluene at room temperature.[4b] However, we found that heating aliphatic substrate **1v** in aqueous solvent system at 100 °C for 24 h afforded a 56% yield of isomer **2v**, which has similar thermodynamic stability to that of **1v**. In addition, (*S*)-**1p** with 92% optical purity rearranged within 2 h in water at 100 °C, but racemic **2p** was obtained (Scheme 3). This evidence is consistent with a mechanism involving an allylic cation, the stability of which strongly influences the rate of the dehydration step. We observed no reaction when we attempted Meyer−Schuster rearrangements of propargylic alcohols in hot water.

Encouraged by the high efficiency of the catalyst-free 1,3-rearrangements of allylic alcohols in hot water, we further investigated 1,5-, 1,7-, and 1,9-rearrangements of allylic alcohols in water without an additional catalyst (Table 4). The 1,5-rearrangement of dienol **3a** in hot water readily afforded a 98% yield of the more conjugated isomer **4a** in which all the double bonds are in the *E* configurations (entry 1). Polyenol **3b**, which has an electron-donating substituent on the phenyl ring, was converted to the desired product at a lower temperature (entry 2), and substrate **3c**, which has an electron-withdrawing substituent, reacted slower than **3a** (entry 3). Phenylethynyl dienol **3d** rearranged to conjugated enyne **4d** (entry 4). Allylic alcohol **3e** could be controlled to undergo the 1,5-rearrangement giving secondary trienol **4e** at 50 °C, because at higher temperature, the reaction produced a mixture of **4e** and a more

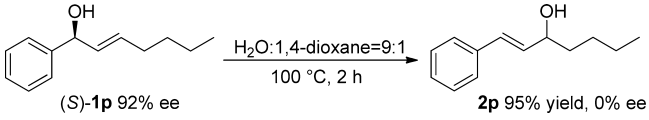
**Table 3. Hot Water-Promoted 1,3-Rearrangements of Acyclic Allylic Alcohols[a]**




| entry | substrate | time (h) | product | yield (%)[b] |
|---|---|---|---|---|
| 1 | **1i** | 12 | **2i** | 98 |
| 2[c] | **1j** | 24 | **2j** | 94 |
| 3 | **1k** | 14 | **2k** | 90 |
| 4[d] | **1l** | 1 | **2l** | 83 |
| 5 | **1m** | 12 | **2m** | 98 |
| 6 | **1n** | 13 | **2n** | 82 (*E* : *Z* = 2.1 : 1)[e] |
| 7 | **1o** | 1 | **2o** | 99 |
| 8 | **1p** | 2 | **2p** | 98 |
| 9 | **1q** | 0.5 | **2q** | 99 |
| 10 | **1r** | 7 | **2r** | 91 |
| 11[d] | **1s** | 2 | **2s** | 94 |
| 12 | **1t** | 1.5 | **2t** | 85 (*E* : *Z* = 2.4 : 1)[e] |
| 13[f] | **1u** | 4 | **2u** | 70[g] |
| 14 | **1v** | 24 | **2v** | 56[h] |

[a]Reaction conditions: 1 mmol substrate in solvent (25 mL, $H_2O$:1,4-dioxane = 9:1), vigorously stirring. [b]Isolated yield. [c]$H_2O$:1,4-dioxane = 4:1. [d]Under a $N_2$ atmosphere. [e]The *E*/*Z* ratio was determined by $^1H$ NMR spectroscopy. [f]$H_2O$:1,4-dioxane = 4:1, 80 °C. [g]23% *cis*-**1u** was obtained. [h]39% of **1v** was recovered.

**Scheme 3. Stereochemical Study of the 1,3-Rearrangement of (*S*)-1p**




thermodynamically stable product with the hydroxyl group at the end of the alkyl chain. Similarly, substrate **3f** rearranged to conjugated trienol **4f** at 50 °C (the quaternary center in the molecule underwent a 1,5-rearrangement during the reaction); both **3f** and **4f** accumulate in apple skin and are produced by the oxidation of the sesquiterpene α-farnesene.[14] The 1,7-rearrangement of polyenol **3g** was complete after 1 h at 100 °C,


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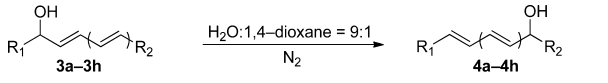
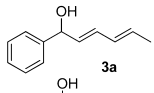
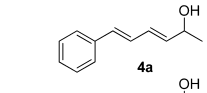
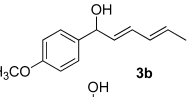
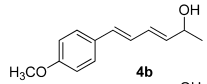
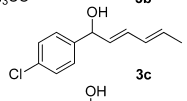
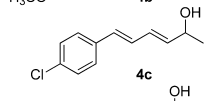
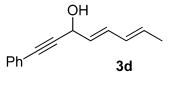
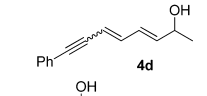
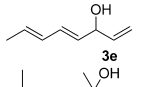
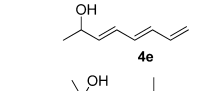
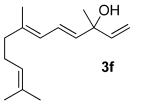
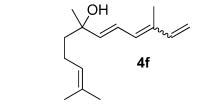
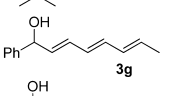
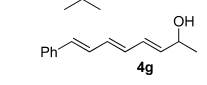
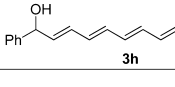
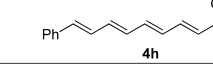
**Table 4. Hot Water-Promoted 1,5-, 1,7-, and 1,9-Rearrangements of Allylic Alcohols**[a]



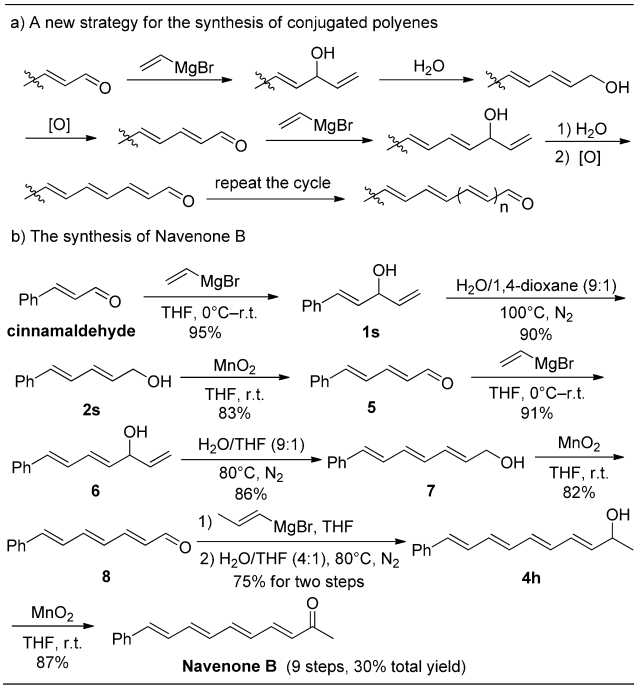

| entry | substrate | temp. (°C)/time (h) | product | yield (%)[b] |
|---|---|---|---|---|
| 1 |  3a | 100/0.25 |  4a | 98 |
| 2 |  3b | 80/1 |  4b | 91 |
| 3 |  3c | 100/1.5 |  4c | 97 |
| 4 |  3d | 100/5 |  4d | 87 (*E* : *Z* = 2 : 1)[c] |
| 5[d] |  3e | 50/2 |  4e | 89 |
| 6[d] |  3f | 50/6 |  4f | 80 (*E* : *Z* = 2.3 : 1)[c] |
| 7 |  3g | 100/1 |  4g | 83 |
| 8[e] |  3h | 80/1 |  4h | 75 |

[a]Reaction conditions: 1 mmol of substrate in solvent (25 mL), vigorously stirring. [b]Isolated yield. [c]The *E*/*Z* ratio was determined by $^1$H NMR spectroscopy. [d]$H_2O$:THF = 9:1. [e]0.5 mmol scale, $H_2O$:1,4-dioxane = 1:1.

and polyenol **3h** (entry 8) underwent 1,9-rearrangement in 1 h at 80 °C. A 1:1 (v/v) mixture of water and 1,4-dioxane was used for the reaction of **3h**, which is very hydrophobic. As the extent of conjugation was increased, the energy barrier for the isomerization decreased, and the reaction became fast even at a temperature below 100 °C.

Because polyene structures are quite stable in hot water, we hypothesized that a polyene natural product could be synthesized through the iteration of a sequence of the three reactions shown in Scheme 4a. This novel synthetic strategy starts with the addition of a vinyl Grignard reagent to an *α*,*β*-unsaturated aldehyde to afford an allylic alcohol with two alkenyl substituents. Treatment of this allylic alcohol with hot water provides an allylic alcohol in which the hydroxy group is rearranged to the end of the polyene. Oxidation of this more-conjugated allylic alcohol affords an *α*,*β*-unsaturated aldehyde, which can then be used as the substrate for the next iteration of the sequence. We demonstrated the efficacy of this strategy by synthesizing navenone B, an alarm pheromone produced under duress by the blind pacific carnivorous opisthobranch mollusk *Navanax inermis* (Scheme 4b). The previously reported syntheses of navenone B have been based on a Wittig-type reaction, the reduction of an alkyne, or transition metal-mediated coupling reactions.[15] In contrast, our synthesis started with a Grignard reaction between cinnamaldehyde and vinylmagnesium bromide. The resulting allylic alcohol was rearranged and then oxidized to give the corresponding *α*,*β*-unsaturated aldehyde, which was subjected to two additional iterations of the reaction sequence to afford navenone B in 30% overall yield. This synthesis has the advantage of using an

**Scheme 4. New Strategy for the Synthesis of Conjugated Polyenes (a) and the Synthesis of Navenone B (b)**




inexpensive starting material (cinnamaldehyde) and only two reagents (the Grignard reagent and $MnO_2$), both of which are commercially available and inexpensive. The rearrangement reaction was carried out in neutral water and gave high *E* selectivity. The chemical yield of the reactions in the third iteration was comparable to that of the first two iterations.

## CONCLUSION

Here, we report for the first time that hot water promotes the 1,*n*-rearrangement of allylic alcohols under neutral conditions. Because no additional catalyst is required, no waste salts are generated, as is the case for reactions catalyzed by Brønsted acids, Lewis acids, or transition metal complexes. The rearranged products were obtained in high to excellent chemical yields and with high *E*:*Z* selectivities in most cases, making this method a valuable addition to the synthetic chemist's toolbox. We incorporated this method into an attractive new strategy for the construction of a polyene natural product using simple, inexpensive reagents. In addition, the unique catalytic effects of water demonstrated here add to our understanding of the behavior of water as a medium for organic reactions and can be expected to facilitate its use in organic synthesis.

## EXPERIMENTAL SECTION

**General Methods.** Unless otherwise mentioned, all reactions were carried out in aerial atmosphere. 1,4-dioxane (HPLC grade) was used as received from Alfa Aesar, and other organic solvents were purified prior to use. Water was purchased from Watson's or from Milli-Q Ultrapure Water Purification System. Substrates were synthesized according to the known procedures. Flash column chromatography was performed using the indicated solvent system on Qingdao-Haiyang silica gel (200–300 mesh). All of the compounds were characterized by $^1$H NMR and $^{13}$C NMR. Peaks recorded are relative to the internal standards: TMS ($\delta$ = 0.00) for $^1$H NMR and $CDCl_3$ ($\delta$ = 77.00) for $^{13}$C NMR spectra. Mass spectral analyses were performed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for low-resolution MS with EI ionization and for high-resolution MS (HRMS) on a QFT-ESI mass spectrometer.

**Preparation of Allylic Alcohols 1a−1v.** Allylic alcohols **1a−1v** were prepared according to previously reported procedures.[16]

*1-(Hex-1-ynyl)cyclohex-2-enol (**1d**).* Colorless oil: $^1$H NMR (400 MHz, $CDCl_3$) $\delta$ 5.80 (dt, $J$ = 9.6, 3.2 Hz, 1H), 5.73 (d, $J$ = 9.6 Hz, 1H), 2.21 (t, $J$ = 6.8 Hz, 2H), 2.06−1.96 (m, 3H), 1.94 (d, $J$ = 2.4 Hz, 1H), 1.93−1.85 (m, 1H), 1.80−1.71 (m, 2H), 1.53−1.34 (m, 4H), 0.91 (t, $J$ = 7.2 Hz, 3H); $^{13}$C NMR (100 MHz, $CDCl_3$) $\delta$ 131.1, 128.9, 84.2, 83.8, 65.1, 38.1, 30.6, 24.6, 21.8, 19.1, 18.3, 13.5; MS (EI, 70 eV) $m/z$ (%) 177 ($M^+$−1, 9), 150 (45), 135 (100), 79 (98), 55 (65), 41(54); HRMS (ESI) for $C_{12}H_{18}O$ calcd for $[M + Na]^+$ $m/z$ 201.1255, found 201.1251.

*2-((E)-Prop-1-en-1-yl)adamantan-2-ol (**1u**).* White solid: mp = 36.5−38 °C; $^1$H NMR (400 MHz, $CDCl_3$) $\delta$ 5.74 (dq, $J$ = 12.0, 1.6 Hz, 1H), 5.56 (dq, $J$ = 11.7, 7.2 Hz, 1H), 2.24 (d, $J$ = 12.1 Hz, 2H), 1.95 (s, 2H), 1.86 (dd, $J$ = 7.2, 1.8 Hz, 3H), 1.85−1.66 (m, 8H), 1.56 (br s, 1H), 1.53 (s, 2H); $^{13}$C NMR (100 MHz, CDCl3) $\delta$ 136.7, 127.4, 75.4, 38.4, 37.9, 34.9, 32.6, 27.0, 26.8, 14.8; HRMS (ESI) for $C_{13}H_{20}O$ calcd for $[M - OH]^+$ $m/z$ 175.1487, found 175.1481.

**Preparation of Allylic Alcohols 3a−3h.** Allylic alcohols **3a−3c**,[17] **3e**,[17] **3f**[18] were prepared according to previously reported procedures.

*(2E,4E)-1-(4-Chlorophenyl)hexa-2,4-dien-1-ol (**3c**).* Colorless oil: $^1$H NMR (400 MHz, $CDCl_3$) $\delta$ 7.33−7.26 (m, 4H), 6.22 (dd, $J$ = 15.2, 10.4 Hz, 1H), 6.03 (ddd, $J$ = 14.8, 10.4, 1.3 Hz, 1H), 5.80−5.61 (m, 2H), 5.17 (d, $J$ = 5.3 Hz, 1H), 2.15 (s, 1H), 1.75 (d, $J$ = 6.7 Hz, 3H); $^{13}$C NMR (100 MHz, $CDCl_3$) $\delta$ 141.4, 133.2, 131.8, 131.6, 131.1, 130.4, 128.5, 127.6, 74.2, 18.1.

*(4E,6E)-1-Phenylocta-4,6-dien-1-yn-3-ol (**3d**).* To a solution of phenylacetylene (1.53 g, 15.0 mmol,) in THF (25 mL) at −78 °C was added *n*-BuLi solution (2.4 M in hexanes, 2.9 mL, 7.0 mmol). The solution was allowed to warm to 0 °C over 1 h and stirred at 0 °C for 30 min. Then the solution was cooled to −78 °C, and (2*E*,4*E*)-hexa-2,4-dienal (505 mg, 5.0 mmol, 95% purity) in THF (10 mL) was added. The reaction mixture was allowed to warm to room temperature over 1 h and stirred at room temperature for 3 h. Diluted aqueous $NH_4Cl$ solution (20 mL) was added to quench the reaction, and the reaction mixture was extracted with EtOAc (2 × 60 mL). The combined organic layers were washed with brine, dried over $MgSO_4$, filtered, and concentrated. The residue was purified by silica gel column chromatography (EtOAc/hexanes = 1:10) to afford the desired product **3d** (978 mg, 99%). Yellow oil: $^1$H NMR (400 MHz, $CDCl_3$) $\delta$ 7.48−7.42 (m, 2H), 7.35−7.28 (m, 3H), 6.44 (dd, $J$ = 15.2, 10.4 Hz, 1H), 6.15−6.05 (m, 1H), 5.88−5.70 (m, 2H), 5.12 (d, $J$ = 6.0 Hz, 1H), 2.00 (br s, 1H), 1.78 (dd, $J$ = 6.4, 1.2 Hz, 3H); $^{13}$C NMR (100 MHz, CDCl3) $\delta$ 132.5, 131.8, 131.7, 130.1, 128.6, 128.5, 128.3, 122.4, 88.1, 86.0, 63.2, 18.2; HRMS (ESI) for $C_{14}H_{14}O$ calcd for $[M + Na]^+$ $m/z$ 221.0942, found 221.0936.

*(4E,6E)-Octa-1,4,6-trien-3-ol (**3e**).* Colorless oil: $^1$H NMR (400 MHz, $CDCl_3$) $\delta$ 6.21 (dd, $J$ = 15.2, 10.4 Hz, 1H), 6.05 (dd, $J$ = 15.2, 11.2 Hz, 1H), 5.90 (ddd, $J$ = 17.2, 10.4, 6.0 Hz, 1H), 5.78−5.68 (m, 1H), 5.58 (dd, $J$ = 15.2, 6.8 Hz, 1H), 5.26 (d, $J$ = 17.2 Hz, 1H), 5.14 (d, $J$ = 10.4 Hz, 1H), 4.64 (m, 1H), 1.76 (d, $J$ = 6.4 Hz, 3H); $^{13}$C NMR (100 MHz, $CDCl_3$) $\delta$ 139.4, 131.4, 131.0, 130.6, 130.5, 115.0, 73.6, 18.1.

*(2E,4E,6E)-1-Phenylocta-2,4,6-trien-1-ol (**3g**).* To a solution of (2*E*,4*E*,6*E*)-octa-2,4,6-trienal (622 mg, 5.0 mmol) in THF (25 mL) was added phenylmagnesium bromide (1.0 M in THF, 6.0 mL, 6.0 mmol) dropwise at 0 °C. The reaction mixture was stirred at 0 °C for 30 min. Then the reaction mixture was allowed to warm to room temperature and further stirred at room temperature for 2 h. Diluted aqueous $NH_4Cl$ solution (20 mL) was added to quench the reaction, and the reaction mixture was extracted with EtOAc (2 × 50 mL). The combined organic layers were washed with brine, dried over $MgSO_4$, filtered, and evaporated under reduced pressure. The residue was purified by silica gel column chromatography (EtOAc/hexanes = 1:10) to afford the title allylic alcohol **3g** (987 mg, 99%). White solid: mp = 73−75 °C; $^1$H NMR (400 MHz, CDCl3) $\delta$ 7.40−7.27 (m, 5H), 6.31 (dd, $J$ = 15.2, 11.2 Hz, 1H), 6.22 (dd, $J$ = 14.8, 10.4 Hz, 1H), 6.14−6.02 (m, 2H), 5.83 (dd, $J$ = 15.2, 6.8 Hz, 1H), 5.79−5.68 (m, 1H), 5.26 (dd, $J$ = 6.8, 3.6 Hz, 1H), 1.92 (d, $J$ = 3.2 Hz, 1H), 1.77 (d, $J$ = 7.2 Hz, 3H); $^{13}$C NMR (100 MHz, CDCl3) $\delta$ 142.9, 134.1, 134.0, 131.5, 131.2, 130.6, 129.2, 128.6, 127.7, 126.2, 74.9, 18.3; HRMS (ESI) for $C_{14}H_{16}O$ calcd for $[M + Na]^+$ $m/z$ 223.1099, found 223.1095.

*(2E,4E,6E,8E)-1-Phenyldeca-2,4,6,8-tetraen-1-ol (**3h**).* To a solution of (2*E*,4*E*,6*E*,8*E*)-deca-2,4,6,8-tetraenal (917 mg, 6.2 mmol) in THF (30 mL) was added phenylmagnesium bromide (1.0 M in THF, 7.4 mL, 7.4 mmol) dropwise at 0 °C. The reaction mixture was stirred at 0 °C for 30 min. Then the reaction mixture was allowed to warm to room temperature and further stirred at room temperature for 2 h. Diluted aqueous $NH_4Cl$ solution (20 mL) was added to quench the reaction, and the reaction mixture was extracted with EtOAc (2 × 50 mL). The combined organic layers were washed with brine, dried over $MgSO_4$, filtered, and evaporated under reduced pressure. The residue was purified by silica gel column chromatography (EtOAc/hexanes = 1:10) to afford the title allylic alcohol **3h** (1.172 g, 99%). Yellow solid: mp = 103−106 °C; $^1$H NMR (400 MHz, $CDCl_3$) $\delta$ 7.42−7.24 (m, 5H), 6.34 (dd, $J$ = 14.8, 10.4 Hz, 1H), 6.27−6.05 (m, 5H), 5.85 (dd, $J$ = 15.2, 6.8 Hz, 1H), 5.74 (m, 1H), 5.26 (dd, $J$ = 6.8, 2.8 Hz, 1H), 1.98 (d, $J$ = 3.6 Hz, 1H), 1.78 (d, $J$ = 7.2 Hz, 3H); $^{13}$C NMR (100 MHz, $CDCl_3$) $\delta$ 142.8, 134.5, 134.0, 133.8, 131.8, 131.1, 130.9, 130.6, 130.1, 128.6, 127.7, 126.2, 74.9, 18.4; HRMS (ESI) for $C_{16}H_{18}O$ calcd for $[M + Na]^+$ $m/z$ 249.1255, found 249.1248.

**General Procedure for Rearrangements of Allylic Alcohols in Table 1.** *3-(Hex-1-ynyl)cyclohex-2-enol (**2d**).* To a round-bottom flask (50 mL) containing the allylic alcohol **1d** (178 mg, 1.0 mmol) was added $H_2O$ (25 mL). The flask was fitted with a condenser, stirred vigorously at the indicated temperature, and monitored by TLC. After completion, the resulting solution was cooled to room temperature. The mixture was extracted with EtOAc (3 × 50 mL), washed with brine, dried over $MgSO_4$, and evaporated under reduced pressure. The residue was purified by silica gel column chromatography (EtOAc/hexanes = 1:10) to afford the desired product **2d** (153 mg, 86%). Colorless oil: $^1$H NMR (400 MHz, $CDCl_3$) $\delta$ 6.00 (m, 1H), 4.23 (s, 1H), 2.30 (t, $J$ = 6.8 Hz, 2H), 2.18−2.00 (m, 2H), 1.88−1.80 (m, 1H), 1.80−1.70 (m, 1H), 1.63−1.55 (m, 2H), 1.53−1.46 (m, 3H), 1.45−1.36 (m, 2H), 0.92 (t, $J$ = 7.2 Hz, 3H); $^{13}$C NMR (100 MHz, $CDCl_3$) $\delta$ 134.0, 124.7, 90.0, 81.1, 65.5, 31.1, 30.8, 29.8, 21.9, 18.9, 18.8, 13.6; HRMS (ESI) for $C_{12}H_{18}O$ calcd for $[M + Na]^+$ $m/z$ 201.1255, found 201.1251.

**General Procedure for Rearrangements of Allylic Alcohols in Table 3.** *1-(Adamantan-2-ylidene)propan-2-ol (**2u**).* To a round-bottom flask (50 mL) containing the substrate **1u** (192 mg, 1.0 mmol) was added 1,4-dioxane (5.0 mL), and then to the solution was added $H_2O$ (20 mL). The flask was fitted with a condenser, stirred vigorously at the indicated temperature, and monitored by TLC. After completion, the resulting solution was cooled to room temperature. The mixture was extracted with EtOAc (3 × 50 mL), washed with brine, dried over $MgSO_4$, and evaporated under reduced pressure. The residue was purified by silica gel column chromatography (EtOAc/hexanes = 1:10) to afford the desired product **2u** (134 mg, 70%). White solid (70%, 134 mg): mp = 35.5−37 °C; $^1$H NMR (400 MHz, $CDCl_3$) $\delta$ 5.13 (d, $J$ = 8.4 Hz, 1H), 4.62 (m, 1H), 2.87 (s, 1H), 2.32 (s, 1H), 1.98−1.65 (m, 12H), 1.30 (d, $J$ = 2.8 Hz, 1H), 1.24 (d, 6.4 Hz, 3H); $^{13}$C NMR (100 MHz, $CDCl_3$) $\delta$ 150.3, 121.4, 63.6, 40.2, 39.8, 39.5, 39.1, 37.1, 32.8, 28.4, 24.2; MS (EI, 70 eV) $m/z$ (%) 192 ($M^+$, 50), 177 (100), 135 (70), 43 (98), 27 (18); HRMS (ESI) for $C_{13}H_{20}O$ calcd for $[M + Na]^+$ $m/z$ 215.1412, found 215.1405.

*Z* isomer of **1u**: white solid; mp = 93−95 °C; $^1$H NMR (400 MHz, $CDCl_3$) $\delta$ 5.87−5.72 (m, 2H), 2.26 (s, 1H), 2.22 (s, 1 H), 1.86 (d, $J$ = 12.5 Hz, 2H), 1.80 (m, 4H), 1.73 (d, $J$ = 4.8 Hz, 3H), 1.72−1.66 (m, 4H), 1.58 (s, 1H), 1.55 (s, 1H), 1.34 (s, 1H); $^{13}$C NMR (100 MHz, CDCl3) $\delta$ 138.0, 124.5, 74.4, 38.0, 38.0, 34.7, 32.8, 27.4, 27.2, 18.2; MS (EI, 70 eV) $m/z$ (%) 192 ($M^+$, 100), 177 (42), 149 (95), 135 (58), 93 (26), 69 (75), 41 (38); HRMS (ESI) for $C_{13}H_{20}O$ calcd for $[M - OH]^+$ $m/z$ 175.1487, found 175.1479.

**Stereochemical Study of the 1,3-Rearrangement of Allylic Alcohol (*S*)-1p.** *Preparation of (S)-**1p**.*[19] $[\alpha]_D^{20}$ +33.4 (c = 1.2, chloroform); HPLC (Chiralcel OD−H) 5:95 *i*-PrOH/Hexane, 1.0


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mL/minute, $\lambda$ = 220 nm, $t_{minor}$ = 6.9 min, $t_{major}$ = 8.4 min, ee = 92.4%. The characterization data for compound (*S*)-**1p** are comparable with that of a previous report.[20]

*1,3-Rearrangement of (S)-**1p**.* To a round-bottom flask (50 mL) containing the substrate (*S*)-**1p** (190 mg, 1 mmol, 92.4% ee) was added 1,4-dioxane (2.5 mL), and then to the solution was added $H_2O$ (22.5 mL). The flask was fitted with a condenser, stirred vigorously at 100 °C, and monitored by TLC. After completion, the resulting solution was cooled to room temperature. The mixture was extracted with EtOAc (3 × 50 mL), washed with brine, dried over $MgSO_4$, and evaporated under reduced pressure. The residue was purified by silica gel column chromatography (EtOAc/hexanes = 1:10) to afford the product **2p** (180 mg, 95% yield, 0% ee indicated by chiral HPLC).

**General Procedure for Rearrangements of Allylic Alcohols in Table 4.** *(3E,5E)-6-(4-Chlorophenyl)hexa-3,5-dien-2-ol (**4c**).* To a 50 mL round-bottom flask containing the substrate **3c** (208 mg, 1.0 mmol) was added 1,4-dioxane (2.5 mL), and then to the solution was added $H_2O$ (22.5 mL). The flask was fitted with a condenser and stirred vigorously for 15 min at the indicated temperature under $N_2$ atmosphere. The resulting solution was cooled to room temperature. The mixture was extracted with EtOAc (3 × 50 mL), washed with brine, dried over $MgSO_4$, and evaporated under reduced pressure. The residue was purified by silica gel column chromatography (EtOAc/hexanes = 1:6) to afford the desired product **4c** (201 mg, 97%). White solid: mp = 94−96 °C; $^1$H NMR (400 MHz, $CDCl_3$) $\delta$ 7.37−7.26 (m, 4H), 6.72 (dd, *J* = 15.6, 10.5 Hz, 1H), 6.49 (d, *J* = 15.7 Hz, 1H), 6.36 (dd, *J* = 15.2, 10.5 Hz, 1H), 5.88 (dd, *J* = 15.2, 6.3 Hz, 1H), 4.50−4.35 (m, 1H), 1.57 (br s, 1H), 1.33 (d, *J* = 6.4 Hz, 3H); $^{13}$C NMR (100 MHz, $CDCl_3$) $\delta$ 138.3, 135.7, 133.1, 131.3, 129.4, 128.8, 128.8, 127.5, 68.5, 23.3; MS (EI, 70 eV) *m*/*z* (%) 208 ($M^+$, 24), 190 (20), 151 (20), 125 (70), 77 (11), 43 (100); HRMS (EI) for $C_{12}H_{13}ClO$ calcd for $[M]^+$ *m*/*z* 208.0655, found 208.0648.

*(3E,5Z)-8-Phenylocta-3,5-dien-7-yn-2-ol (**4d-1**).* Slight yellow oil: $^1$H NMR (400 MHz, $CDCl_3$) $\delta$ 7.50−7.43 (m, 2H), 7.35−7.29 (m, 3H), 6.84 (dd, *J* = 15.2 Hz, 11.2 Hz, 1H), 6.42 (t, *J* = 10.8 Hz, 1H), 5.95 (dd, *J* = 15.2 Hz, 6.4 Hz, 1H), 5.67 (d, *J* = 10.8 Hz, 1H), 4.45 (m, 1H), 1.75 (br s, 1H), 1.33 (d, *J* = 6.4 Hz, 3H); $^{13}$C NMR (100 MHz, $CDCl_3$) $\delta$ 140.6, 139.1, 131.4, 128.3, 128.2, 126.6, 123.3, 109.5, 95.8, 86.4, 68.4, 23.1; MS (EI, 70 eV) *m*/*z* (%) 198 ($M^+$, 8), 197 (14), 183 (45), 153 (47), 105 (92), 77 (58), 43 (100); HRMS (ESI) for $C_{14}H_{14}O$ calcd for $[M + Na]^+$ *m*/*z* 221.0942, found 221.0934.

*(3E,5E)-8-Phenylocta-3,5-dien-7-yn-2-ol (**4d-2**).* Slight yellow oil: $^1$H NMR (400 MHz, $CDCl_3$) $\delta$ 7.47−7.40 (m, 2H), 7.35−7.28 (m, 3H), 6.66 (dd, *J* = 15.6 Hz, 10.8 Hz, 1H), 6.31 (dd, *J* = 15.2, 10.8 Hz, 1H), 5.87 (dd, *J* = 15.6 Hz, 6.4 Hz, 1H), 5.83 (d, *J* = 15.6 Hz, 1H), 4.40 (m, 1H), 1.62 (br s, 1H), 1.31 (d, *J* = 6.4 Hz, 3H); $^{13}$C NMR (100 MHz, $CDCl_3$) $\delta$ 140.9, 139.7, 131.4, 128.6, 128.3, 128.1, 123.3, 111.4, 92.1, 88.7, 68.2, 23.2; HRMS (ESI) for $C_{14}H_{14}O$ calcd for $[M + Na]^+$ *m*/*z* 221.0942, found 221.0934.

*(3E,5E)-Octa-3,5,7-trien-2-ol (**4e**).* Colorless oil (89%, 110 mg): $^1$H NMR (400 MHz, $CDCl_3$) $\delta$ 6.41−6.30 (m, 1H), 6.27−6.17 (m, 3H), 5.80−5.72 (m, 1H), 5.22 (dd, *J* = 16.4, 1.6 Hz, 1H), 5.10 (dd, *J* = 10.0, 1.6 Hz, 1H), 4.35 (m, 1H), 1.82 (s, 1H), 1.28 (d, *J* = 6.4 Hz, 3H); $^{13}$C NMR (100 MHz, $CDCl_3$) $\delta$ 137.8, 136.8, 133.5, 132.3, 129.3, 117.5, 68.4, 23.2; MS (EI, 70 eV) *m*/*z* (%) 124 ($M^+$, 13), 91 (10), 81 (31), 55 (16), 43 (100); HRMS (EI) for $C_8H_{12}O$ calcd for $[M]^+$ *m*/*z* 124.0888, found 124.0890.

*(3E,5E,7E)-8-Phenylocta-3,5,7-trien-2-ol (**4g**).* A slight yellow solid (83%, 166 mg): mp =104.5−106.5 °C; $^1$H NMR (400 MHz, $CDCl_3$) $\delta$ 7.40 (d, *J* = 7.2 Hz, 2H), 7.31 (d, *J* = 7.6 Hz, 2H), 7.22 (t, *J* = 7.6 Hz,1H), 6.82 (dd, *J* = 15.6 Hz, 10.0 Hz, 1H), 6.56 (d, *J* = 15.6 Hz, 1H), 6.44−6.26 (m, 3H), 5.80 (dd, *J* = 13.6, 6.8 Hz, 1H), 4.40 (m, 1H), 1.52 (br s, 1H), 1.32 (d, *J* = 6.4 Hz, 3H); $^{13}$C NMR (100 MHz, $CDCl_3$) $\delta$ 137.5, 137.2, 133.4, 132.7, 132.4, 129.7, 128.8, 128.6, 127.6, 126.3, 68.6, 23.3; MS (EI, 70 eV) *m*/*z* (%) 200 ($M^+$, 63), 128 (80), 91 (100), 77 (24), 43 (63); HRMS (ESI) for $C_{14}H_{16}O$ calcd for $[M + Na]^+$ *m*/*z* 223.1099, found 223.1092.

**Synthesis of Navenone B.** To a solution of cinnamaldehyde (1.078 g, 8.0 mmol, 98% purity) in THF (25 mL) was added vinylmagnesium bromide (1.0 M in THF, 9.6 mL, 9.6 mmol) dropwise at 0 °C. The reaction mixture was stirred at 0 °C for 30 min. Then the reaction mixture was allowed to warm to room temperature and further stirred at room temperature for 2 h. Diluted aqueous $NH_4Cl$ solution was added to quench the reaction, and the reaction mixture was extracted with EtOAc (3 × 50 mL). The combined organic layers were washed with brine, dried over $MgSO_4$, filtered and evaporated under reduced pressure. The residue was purified by silica gel column chromatography (EtOAc/hexanes = 1:10) to afford the desired product **1s** (1.237 g, 96%): $^1$H NMR (400 MHz, $CDCl_3$) $\delta$ 7.41−7.35 (m, 2H), 7.34−7.28 (m, 2H), 7.27−7.21 (m, 1H), 6.61 (d, *J* = 15.6 Hz, 1H), 6.23 (dd, *J* = 16.0, 6.4 Hz, 1H), 5.97 (ddd, *J* = 17.2, 10.4, 6.0 Hz, 1H), 5.34 (dt, *J* = 17.2, 1.2 Hz, 1H), 5.19 (d, *J* = 10.4, 1.2 Hz, 1H), 4.81 (br s, 1H), 1.89 (s, 1H); $^{13}$C NMR (100 MHz, $CDCl_3$) $\delta$ 139.2, 136.5, 130.8, 130.3, 128.5, 127.7, 126.5, 115.4, 73.8. The characterization data for this compound matched that of a previous report.[21]

To a solution of (*E*)-1-phenylpenta-1,4-dien-3-ol **1s** (480 mg, 3.0 mmol) in 1,4-dioxane (7.5 mL) was added $H_2O$ (67.5 mL). The flask was fitted with a condenser and stirred vigorously at 100 °C under $N_2$ atmosphere for 1 h. After completion, the resulting solution was cooled to room temperature. Brine (25 mL) was added, and the mixture was extracted with EtOAc (2 × 100 mL), washed with brine, dried over $MgSO_4$, and evaporated under reduced pressure. The residue was purified by silica gel column chromatography (EtOAc/hexanes = 1:6) to afford the desired product **2s** (434 mg, 90%) as a white solid: $^1$H NMR (400 MHz, $CDCl_3$) $\delta$ 7.4−7.2 (m, 5H). 6.79 (dd, *J* = 15.6 Hz, 10.4 Hz, 1H), 6.56 (d, *J* = 15.6, 1H), 6.43 (dd, *J* = 15.2 Hz, 10.8 Hz, 1H), 5.97 (dt, *J* = 15.2 Hz, 6.0 Hz, 1H), 4.25 (d, *J* = 5.6 Hz, 2H), 1.43 (br s, 1H); $^{13}$C NMR (100 MHz, $CDCl_3$) $\delta$ 137.1, 132.8, 132.5, 131.6, 128.6, 128.1, 127.6, 126.4, 63.4. The characterization data for this compound matched that of a previous report.[22]

To a solution of the alcohol **2s** (660 mg, 4.1 mmol) in THF (40 mL) was added $MnO_2$ (3.56 g, 41.0 mmol). The reaction mixture was stirred for 1 h before being filtered through a pad of celite to remove inorganic compound. The filtrate was concentrated, and the residue was purified by silica gel column chromatography (EtOAc/hexanes = 1:10) to give the aldehyde **5** (544 mg, 83%): $^1$H NMR (400 MHz, $CDCl_3$) $\delta$ 9.62 (d, *J* = 8.0 Hz, 1H), 7.53−7.48 (m, 2H), 7.42−7.34 (m, 3H), 7.27 (ddd, *J* = 14.8, 7.2, 2.8 Hz 1H), 7.04−6.99 (m, 2H), 6.27 (dd, *J* = 15.2, 8.0 Hz, 1H); $^{13}$C NMR (100 MHz, $CDCl_3$) $\delta$ 193.6, 152.0, 142.4, 135.5, 131.6, 129.7, 128.9, 127.5, 126.1. The characterization data for this compound matched that of a previous report.[23]

To a solution of aldehyde **5** (901 mg, 5.7 mmol) in THF (30 mL) was added vinylmagnesium bromide (1.0 M in THF, 6.8 mL, 6.8 mmol) dropwise at 0 °C. The reaction mixture was stirred at 0 °C for 30 min. Then the reaction mixture was allowed to warm to room temperature and further stirred at room temperature for 2 h. Diluted aqueous $NH_4Cl$ solution was added to quench the reaction, and the reaction mixture was extracted with EtOAc (3 × 50 mL). The combined organic layers were washed with brine, dried over $MgSO_4$, filtered, and evaporated under reduced pressure. The residue was purified by silica gel column chromatography (EtOAc/hexanes = 1:6) to afford the desired product **6** (960 mg, 91%). Slight yellow solid: mp = 70.5−72 °C; $^1$H NMR (400 MHz, CDCl3) $\delta$ 7.42−7.37 (m, 2H), 7.35−7.28 (m, 2H), 7.25−7.20 (m, 1H), 6.78 (dd, *J* = 15.6, 10.4 Hz, 1H), 6.57 (d, *J* = 15.6 Hz, 1H), 6.43 (dd, *J* = 15.2, 10.4 Hz, 1H), 5.94 (ddd, *J* = 17.2, 10.4, 6.0 Hz, 1H), 5.84 (dd, *J* = 15.2, 6.4 Hz, 1H), 5.34 (dt, *J* = 17.2, 1.6 Hz, 1H), 5.18 (dt, *J* = 10.4, 1.6 Hz, 1H), 4.78−4.70 (m, 1H), 1.66 (d, *J* = 4.4 Hz, 1H); $^{13}$C NMR (100 MHz, CDCl3) $\delta$ 139.1, 137.0, 134.2, 133.1, 131.1, 128.6, 128.0, 127.6, 126.4, 115.3, 73.5; MS (EI, 70 eV) *m*/*z* (%) 186 ($M^+$, 17), 167 (8), 141 (13), 115 (51), 91 (100), 82 (33), 55 (77); HRMS (ESI) for $C_{13}H_{14}O$ calcd for $[M - H]^-$ *m*/*z* 185.0966, found 185.0977.

To a solution of allylic alcohol **6** (558 mg, 3.0 mmol) in THF (15 mL) was added $H_2O$ (135 mL). The flask was fitted with a condenser and stirred vigorously at 80 °C under $N_2$ atmosphere for 4 h. The resulting solution was cooled to room temperature. Brine (50 mL) was added. Then the mixture was extracted with EtOAc (2 × 150 mL), washed with brine, dried over $MgSO_4$, and evaporated under reduced pressure. The residue was purified by silica gel column chromatography (EtOAc/hexanes = 1:5) to afford the desired product **7** (479


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mg, 86%). White solid: mp = 93.5−96 °C; $^1$H NMR (400 MHz, $CDCl_3$) $\delta$ 7.40 (d, $J$ = 7.6 Hz, 2H), 7.32 (t, $J$ = 7.2 Hz, 2H), 7.22 (t, $J$ = 7.2 Hz, 1H), 6.82 (dd, $J$ = 15.6, 9.6 Hz, 1H), 6.57 (d, $J$ = 15.6 Hz, 1H), 6.45−6.29 (m, 3H), 5.95−5.85 (m, 1H), 4.23 (m, 2H), 1.52 (s, 1H); $^{13}$C NMR (100 MHz, $CDCl_3$) $\delta$ 137.2, 133.4, 132.8, 132.4, 132.3, 131.5, 128.8, 128.6, 127.6, 126.3, 63.4 ($CH_2$).

To a solution of the alcohol 7 (372 mg, 2.0 mmol) in THF (50 mL) was added $MnO_2$ (1.74 g, 20 mmol). The reaction mixture was stirred for 1 h before being filtered through a pad of celite to remove inorganic compound. The filtrate was concentrated, and the residue was purified by silica gel column chromatography (EtOAc/hexanes = 1:10) to give the aldehyde **8** (303 mg, 82%) as a yellow solid: $^1$H NMR (400 MHz, CDCl3) $\delta$ 9.58 (d, $J$ = 8.0 Hz, 1H), 7.47−7.42 (m, 2H), 7.38−7.32 (m, 2H), 7.32−7.24 (m, 1H), 7.17 (dd, $J$ = 15.2, 11.2 Hz, 1H), 6.94−6.76 (m, 3H), 6.55 (dd, $J$ = 14.0, 11.2 Hz, 1H), 6.18 (dd, $J$ = 15.2, 8.0 Hz, 1H); $^{13}$C NMR (100 MHz, CDCl3) $\delta$ 193.4, 151.7, 142.7, 138.3, 136.2, 131.1, 130.1, 128.8, 127.6, 126.9. The characterization data for this compound matched that of a previous report.[24]

To a solution of aldehyde **8** (253 mg, 1.3 mmol) in THF (10 mL) was added prop-1-enylmagnesium bromide (0.5 M in THF, 3.2 mL, 1.6 mmol) dropwise at 0 °C. The reaction mixture was stirred at 0 °C for 30 min. Then the reaction mixture was allowed to warm to room temperature and further stirred at room temperature for 2 h. Diluted aqueous $NH_4Cl$ solution was added to quench the reaction, and the reaction mixture was extracted with EtOAc (3 × 20 mL). The combined organic layers were washed with brine, dried over $MgSO_4$, filtered, and evaporated under reduced pressure. The residue was purified by passing it through a short silica gel column chromatography (EtOAc/hexanes = 1:4) to afford a yellow solid (1.17 mmol, 266 mg), which was directly used in the next step.

To a solution of the yellow solid (1.17 mmol, 266 mg) in THF (11 mL) was added $H_2O$ (44 mL). The flask was fitted with a condenser and stirred vigorously at 80 °C under $N_2$ atmosphere for 1 h. The resulting solution was cooled to room temperature. Brine (20 mL) was added. Then the mixture was extracted with EtOAc (2 × 80 mL), washed with brine, dried over $MgSO_4$, and evaporated under reduced pressure. The residue was purified by silica gel column chromatography (EtOAc/hexanes = 1:3) to afford the desired product **4h** (196 mg, 75%) as a yellow solid: mp = 124−125.5 °C; $^1$H NMR (400 MHz, $CDCl_3$) $\delta$ 7.40 (d, $J$ = 7.6 Hz, 2H), 7.31 (d, $J$ = 7.6 Hz, 2H), 7.22 (t, $J$ = 7.2 Hz,1H), 6.84 (dd, $J$ = 15.6 Hz, 9.6 Hz, 1H), 6.57 (d, $J$ = 15.6 Hz, 1H), 6.46−6.22 (m, 5H), 5.79 (dd, $J$ = 13.6, 6.8 Hz, 1H), 4.39 (m, 1H), 1.47 (d, $J$ = 4.0 Hz, 1H), 1.31 (d, $J$ = 6.4 Hz, 3H); $^{13}$C NMR (100 MHz, $CDCl_3$) $\delta$ 137.5, 137.3, 133.5, 133.3, 133.2, 132.7, 132.3, 129.8, 129.0, 128.6, 127.5, 126.3, 68.6, 23.3. The characterization data for this compound matched that of a previous report.[25]

To a solution of the alcohol **4h** (113 mg, 0.5 mmol) in THF (10 mL) was added $MnO_2$ (435 mg, 5 mmol). The reaction mixture was stirred for 1 h before being filtered through a pad of celite to remove inorganic compound. The filtrate was concentrated, and the residue was purified by silica gel column chromatography (EtOAc/hexanes = 1:5) to give the desired product navenone B (99 mg, 87%). Yellow solid: mp =136−138 °C; $^1$H NMR (400 MHz, $CDCl_3$) $\delta$ 7.43 (d, $J$ = 7.6 Hz, 2H), 7.34 (t, $J$ = 7.6 Hz, 2H), 7.28−7.26 (m, 1H), 7.19 (dd, $J$ = 15.2, 11.2 Hz, 1H), 6.88 (dd, $J$ = 15.6, 10.8 Hz, 1H), 6.75−6.65 (m, 2H), 6.60 (dd, $J$ = 14.8, 10.8 Hz, 1H), 6.49−6.33 (m, 2H), 6.16 (d, $J$ = 15.6 Hz, 1H), 2.29 (s, 3H); $^{13}$C NMR (100 MHz, $CDCl_3$) $\delta$ 198.3, 143.2, 141.6, 137.7, 136.9, 135.3, 132.2, 130.5, 129.9, 128.7, 128.5, 128.2, 126.6, 27.4.

## ■ ASSOCIATED CONTENT

### Supporting Information

$^1$H and $^{13}$C NMR spectra of products in Table 1, Table 3, Table 4, and Scheme 4. This material is available free of charge via the Internet at http://pubs.acs.org.

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### Notes

The authors declare no competing financial interest.

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