Palladium-Catalyzed Cascade Wacker/Allylation Sequence with Allylic Alcohols Leading to Allylated Dihydropyrones

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ABSTRACT: We describe a cascade Wacker/allylation sequence of \( \beta \)-hydroxy yrones by directly using simple allylic alcohols. This palladium(II)-catalyzed reaction occurs under mild conditions (0 \(^\circ\) C to room temperature) and provides a new and efficient synthetic method for the preparation of allylated dihydropyrones. The regiochemical outcomes are consistent with a reaction pathway that includes an insertion/\( \beta \)-OH elimination sequence to form the allylic moiety. A remarkable changeover from allyl to formylethyl products occurs under the simple action of LiBr.

INTRODUCTION

Allylic alcohols are well recognized as versatile building blocks for the construction of functionalized carbon frameworks by palladium-catalyzed reactions, including nucleophilic allylic substitutions and Mizoroki–Heck reactions. These reactions are also quite attractive from the viewpoint of green and atom economically favorable processes. In contrast to the numerous examples of allylic substitution of nucleophiles via \( \pi \)-allylpalladium intermediates or introduction of formylethyl groups through Mizoroki–Heck reactions, allylations via Mizoroki–Heck reactions that directly use allylic alcohols have been relatively less explored, despite the straightforwardness of this process (Scheme 1).

Recently, in the course of studies aimed at the synthesis of functionalized dihydropyrones, we discovered, by chance, a new cascade reaction with allyl alcohol (Scheme 2). In this reaction, \( \beta \)-hydroxy ynone 1 underwent a palladium-catalyzed cascade sequence, including Wacker-type cyclization and subsequent allylation with allyl alcohol (cascade Wacker/allylation sequence) under mild conditions (0 \(^\circ\) C to room temperature), providing allyl dihydropyrone 2a in good yield. Herein, we report this cascade Wacker/allylation sequence, which offers a new and efficient entry to functionalized dihydropyrones. We also report that addition of LiBr allowed remarkable product changeover from allyl dihydropyrone 2a to formylethyl derivative 3, provided via a conventional Mizoroki–Heck reaction (Scheme 2).

RESULTS AND DISCUSSION

We first examined a cascade Wacker/Mizoroki–Heck sequence with allyl alcohol according to the conditions for a related reaction reported by Gouverneur and co-workers. In this reaction, readily available \( \beta \)-hydroxy ynone 1 (for details, see the Supporting Information) was subjected to catalytic amounts...
of (MeCN)2PdCl2 and Cu(OAc)2·H2O (10 mol % each) in the presence of LiBr (4.0 equiv) to provide aldehyde 3 in 72% yield, as anticipated (Table 1, entry 1). Unexpectedly, in the absence of LiBr, the reaction resulted in the exclusive formation of allyl dihydropyrrone 2a in 78% yield; no aldehyde 3 was observed, even in the crude mixture, as judged by 1H NMR analysis (entry 2). These results indicate that LiBr plays an important role in the remarkable changeover between products 3 and 2a. It is likely that both components of LiBr contribute to the formation of 3 in good yield. Indeed, formation of aldehyde 3 in the absence of allylated 2a also proceeded in lower yields in the presence of other additives, such as LiCl, tetrabutylammonium salts, NaBr, and KBr (entries 3–8), but not in the presence of the more Lewis acidic LiBF4 (entry 9) (for details, see the Supporting Information).

Further experiments were then conducted to elucidate the details of this cascade Wacker/allylation sequence. Control experiments established that allylated product 2a was observed only in the presence of (MeCN)2PdCl2, irrespective of the introduction of oxygen and Cu(OAc)2·H2O (Table 2). Among the Pd(II) complexes we have examined, (MeCN)2PdCl2 and (PhCN)2PdBr2 were effective precatalysts (Table 3). It is also of interest to note that the reaction with (PhCN)2PdBr2 resulted in the exclusive formation of 2a in 70% yield, with no aldehyde 3 observed, despite the presence of bromide in the reaction system (entry 4). Furthermore, the use of Pd(OAc)2 and Pd(OCCF3)2 resulted in the formation of protonated dihydropyrrone 4 in 5 and 71% yields, respectively (entries 5 and 6). The reaction did not proceed with Pd(0) complexes, such as Pd(PPh3)4 and Pd2(dba)3·CHCl3 (entries 7 and 8). The use of various organic solvents, such as Et2O, CH2Cl2, tetrahydrofuran (THF), toluene, dimethylformamide (DMF), MeOH, and MeCN, for this transformation provided 2a in 42–69% yields (for details, see the Supporting Information).

We next investigated the effect of the allylic alcohol structure on the cascade Wacker/allylation sequence (Table 4). Secondary and tertiary vinyl carbinols, such as 3-buten-2-ol and 2-methyl-3-buten-2-ol, underwent the cascade Wacker/allylation sequence to provide the corresponding products 2b and 2c in 57 and 51% yields, respectively (entries 1 and 2); no aldehyde or regioisomeric products of the Mizoroki–Heck reaction were formed. In these reactions, only representative γ-isomers were formed, which strongly indicates that the reaction proceeds through insertion/β-OH elimination, rather than allylation via a π-allyl palladium intermediate.2c,10 Reaction with methallyl alcohol proceeded at 0 °C to afford the corresponding product 2d in 29% yield (entry 3). A terminal substituent in allylic alcohols retarded the reaction; E-crotyl alcohol was found to afford the corresponding product 2e as a single regioisomer, with a decreased yield of 21% (entry 4). A limitation of this cascade sequence is that allylic alcohols having a trisubstituted alkene provided poor results; the reaction with sterically congested prenyl alcohol afforded undesired dihydropyrrone 5 (Figure 1) in 13% yield, instead of reverse-prenyl product 2f (entry 5).

Table 1. Effect of Additives

| entry | additive | 2a | 3 |
|-------|----------|----|---|
| 1     | LiBr     | 0  | 72 (67) |
| 2     | –        | 78 (70) | 0 |
| 3     | LiCl     | 0  | 13 |
| 4     | n-Bu4NBr | 0  | 34 |
| 5     | n-Bu4NCl | 0  | 50 |
| 6     | n-Bu4NHSO4 | 0  | 13 |
| 7     | NaBr     | 0  | 26 |
| 8     | KBr      | 0  | 23 |
| 9     | LiBF4    | 41 | 0 |

*All reactions were conducted with 0.194 mmol of 1 in DME (1.0 mL). *Determined by 1H NMR analysis using an internal standard. *Ynone 1 was recovered in 29% yield. Ynone 1 was recovered in 25% yield.

Table 2. Screening of the Reaction Conditions for the Cascade Wacker/Allylation Sequence

| entry | Pd     | Cu | atmosphere | yield (%) |
|-------|--------|----|------------|-----------|
| 1     | +      | +  | Ar         | 70        |
| 2     | +      | –  | O2         | 56        |
| 3     | +      | –  | Ar         | 69        |
| 4     | –      | +  | O2         | 0         |
| 5     | –      | +  | Ar         | 0         |
| 6     | –      | –  | O2         | 0         |
| 7     | –      | –  | Ar         | 0         |

*All reactions were conducted with 0.194 mmol of 1 in DME (1.0 mL). *Determined by 1H NMR analysis using an internal standard.

Table 3. Screening of Palladium Complexes

| entry | Pd complex | time (h) | 2a yield (%) | recovered 1 |
|-------|------------|---------|--------------|-------------|
| 1     | (MeCN)2PdCl2 | 23.5 | 69 (64) | 0 |
| 2     | (Ph3P)2PdCl2 | 23.5 | 0  | 99 |
| 3     | PdCl2       | 23.5 | 30 | 0  | 51 |
| 4     | (PhCN)2PdBr2 | 1  | 70 | 0  |
| 5     | Pd(OAc)2    | 22.5 | 5  | 83 |
| 6     | Pd(OCCF3)2  | 22.5 | 71| 0  |
| 7     | Pd(PPh3)4   | 16 | 0  | >99 |
| 8     | Pd(dba)2·CHCl3 | 16 | 0  | >99 |

*All reactions were conducted with 0.194 mmol of 1 in DME (1.0 mL). *Determined by 1H NMR analysis using an internal standard. *Isolated yield is given in parentheses.
The cascade Wacker/allylation sequence was applicable to the construction of several allylated dihydropyrones (Table 5). The cascade reaction proceeded with ynone \( \text{6} \) bearing a siloxy functional group to give \( \text{7} \) in 74% yield (entry 1). Hydroxy ynones \( \text{8} \) and \( \text{10} \) bearing a sterically congested substituent (phenyl or TMS group) on the terminus of the alkyne underwent the reaction smoothly to provide \( \text{9} \) and \( \text{11} \) in moderate yields of 55 and 57%, respectively (entries 2 and 3). Moreover, the cascade sequence with \( \text{12} \) having a terminal alkyne afforded expected dihydropyrene \( \text{13} \) in 37% yield (entry 4). Primary alcohol \( \text{14} \) also underwent the cascade reaction to provide \( \text{15} \) in 75% yield (entry 5). In most cases, reactions at 0 °C could suppress side reactions and provided higher yield of products (entries 2–5). In contrast, cyclization using 2-(3-phenylpropynoyl)phenol \( \text{16} \) did not proceed to give 3-allyl flavone-type scaffold \( \text{17} \) but provided the unreacted substrate probably due to the less nucleophilic phenolic hydroxy group (entry 6).

A plausible mechanism for the present cascade reaction is proposed in Scheme 3. \( \beta \)-Hydroxy ynone \( \text{A} \) undergoes oxypalladation with palladium(II) species, leading to alkenylpalladium(II) intermediate \( \text{B} \) bearing a dihydropyrene scaffold, which engages in sequential insertion of the C\(-\)C bond of allyl alcohol to generate alkylpalladium(II) intermediate \( \text{C} \). Then, the presence of excess LiBr may facilitate \( \beta \)-H elimination probably through coordination of LiBr as a Lewis acid to the primary hydroxy group. Palladium(0) species could then be oxidized by Cu(II)/O\(_2\) to regenerate PdX\(_2\). On the other hand, in the absence of LiBr, \( \text{C} \) or its cationic intermediate \( \text{C}^+ \) undergoes \( \beta \)-OH elimination to form allylated dihydropyrene \( \text{F} \) along with Pd(OH)Cl. No reoxidant is required for this process, as PdX\(_2\) could be regenerated through dehydration of Pd(OH)Cl with a proton.
CONCLUSIONS

In conclusion, we have described a new cascade Wacker/allylation sequence starting from $\beta$-hydroxy ynones and occurring under mild conditions in a single operation by directly using allylic alcohols. This new reaction offers a very convenient entry to functionalized dihydropyrones of synthetic value. Additionally, a remarkable changeover from allyl and formylethyl products occurs under the simple action of LiBr. Further studies of the present cascade reaction, including generalities of direct allylation with aryl- or alkenylmetals and LiBr-promoted product changeover, as well as its application to the synthesis of natural products, are in progress.

EXPERIMENTAL SECTION

General Information. IR spectra were recorded on a JASCO FT/IR-6100 spectrometer and reported in wavenumber (cm$^{-1}$). Proton nuclear magnetic resonance ($^1$H NMR) spectra were recorded on a Bruker AVANCE-400 NMR spectrometer (400 MHz). Chemical shifts of all compounds were reported in ppm, relative to the residual undeuterated solvent (chloroform-$d$ as $\delta = 7.26$). $^1$H NMR data were reported as follows: chemical shifts, integration, multiplicity (s = singlet, d = doublet, t = triplet, q = quartet, m = multiplet, br = broadened), coupling constant(s), and assignment. Carbon nuclear magnetic resonance ($^{13}$C NMR) spectra were recorded on a Bruker AVANCE-400 spectrometer (100 MHz). Chemical shifts were reported in ppm, relative to the solvent (CDCl$_3$ as $\delta = 77.0$). High-resolution mass spectra (HRMS) were recorded on an Applied Biosystems Mariner electrospray ionization-time-of-flight (ESI-TOF) spectrometer and are reported in m/z. Reactions were monitored by thin-layer chromatography (TLC) on 0.25 mm silica gel-coated glass plates, 60F$_{254}$ (Merck, #1.05715.0009), using UV light (254 nm) as the visualizing agent and 7% ethanoic phosphomolybdic acid, $p$-anisaldehyde solution in H$_2$SO$_4$/AcOH, ninhydrin solution in n-BuOH/H$_2$O/AcOH, a solution of cerium (IV) sulfate tetrahydrate and (NH$_4$)$_6$Mo$_7$O$_{24}$·4H$_2$O in H$_2$O/H$_2$SO$_4$, or a solution of KMnO$_4$ in 1 M NaOH and heated as developing agents. Silica gel 60 (particle size 0.0063–0.021 mm, Kanto, #37565-84) was used for open-column chromatography. Silica gel 60N (spherical, neutral, particle size 0.04–0.05 mm, Kanto, #37563-79) was used for flash-column chromatography. Preparative TLC separations were carried out on 0.5 mm silica gel plates 60F$_{254}$ (Merck, #1.05744.0009). Dehydrated THF, Et$_2$O, and CH$_2$Cl$_2$ were purchased from Kanto Chemical Co., Inc. DMF and DME were distilled from CaH$_2$. Oct-3-yn-2-one. To a solution of 1-hexyne (30.0 mL, 261 mmol) in THF (130 mL) was added n-BuLi (2.6 M in hexane, 111 mL, 289 mmol) at $-78^\circ$C under an argon atmosphere. The reaction mixture was stirred at $-78^\circ$C for 1 h. To the reaction mixture was added 4-acetylmorpholine (33 mL, 285 mmol) at $-78^\circ$C, and the resulting mixture was allowed to warm to 0°C. The solution was stirred at 0°C for 30 min. The reaction was quenched with a saturated aqueous solution of NH$_4$Cl at 0°C, and the resulting mixture was allowed to warm to room temperature. The aqueous layer was extracted with Et$_2$O. The organic layer was dried over anhydrous Na$_2$SO$_4$ and concentrated. The residue was purified by distillation (9 mm Hg, 62°C) to give oct-3-yn-2-one (21.6 g, 67%) as a yellow oil.

$^1$H NMR was identical to that reported previously for the corresponding compound.$^{13}$ $^1$H NMR (CDCl$_3$, 400 MHz) $\delta$ (ppm) 2.36 (2H, t, $J = 7$ Hz, CCCH$_2$–), 2.32 (3H, s, COCH$_3$), 1.61–1.51 (2H, m, CH$_2$CH$_2$CH$_2$–), 1.49–1.37 (2H, m, CH$_2$CH$_2$CH$_2$–), 0.928 (3H, t, $J = 7$ Hz, CH$_3$CH$_2$CH$_2$–); $^{13}$C NMR (CDCl$_3$, 100 MHz) $\delta$ (ppm) 185.0, 94.2, 81.4, 32.8, 29.7, 21.9, 18.6, 13.5. Hydroxy Ynone 1. To a solution of diisopropylamine (8.4 mL, 60 mmol) in THF (300 mL) was added n-BuLi (2.6 M in hexane, 23 mL, 60 mmol) at $-78^\circ$C under an argon atmosphere. The reaction mixture was stirred at $-78^\circ$C for 1
h. To the reaction mixture was added oct-3-yn-2-one (8.6 mL, 60 mmol) at −78 °C. After being stirred at −78 °C for 2 h, a solution of 3-phenylpropanol (6.6 mL, 50 mmol) in THF (500 mL) was added dropwise to the resulting mixture. After being stirred at −78 °C for 15 min, the reaction was quenched with a saturated aqueous solution of NH₄Cl at −78 °C, and the resulting mixture was allowed to warm to room temperature. The aqueous layer was extracted with Et₂O. The organic layer was dried over anhydrous Na₂SO₄ and concentrated. The residue was purified by silica gel column chromatography (hexane/EtOAc = 3:1) to give I (10.5 g, 83%) as a yellow oil. IR (KBr) νmax (cm⁻¹) 3440, 2932, 2211, 1668, 1455; ¹H NMR (CDCl₃, 400 MHz) δ (ppm) 7.32–7.16 (5H, m, Ph), 6.17–6.07 (1H, m, HOC=CH), 2.86–2.65 (SH, m, PhCH₂–, COCH₂OH), 2.37 (2H, t, J = 7 Hz, CCCH₂–), 1.89–1.66 (2H, m, PhCH₂CH₂–), 1.61–1.51 (2H, m, CH₂CH₂CH₂–), 1.48–1.36 (2H, m, CH₂CH₂CH₂–), 0.92 (3H, t, J = 7.5 Hz, CH₃–); ¹³C NMR (CDCl₃, 100 MHz) δ (ppm) 187.6, 141.7, 128.42, 128.38, 125.9, 95.8, 80.9, 66.5, 52.8, 37.9, 31.7, 29.6, 21.9, 18.6, 13.4; HRMS (ESI, positive): calcd for C₁₇H₂₂O₂Na (M + Na), 495.1252; found, 495.1250.

**Cascade Wacker/Allylation Sequence (Scheme 2; Table 1, Entry 2).** Dihydropyrrone 2a. To a solution of 1 (50.0 mg, 0.194 mmol) and allyl alcohol (0.125 mL, 1.94 mmol) in THF (1 mL) was added Cu(OAc)₂·H₂O (3.9 mg, 0.019 mmol) at room temperature under an argon atmosphere. The vessel was then degassed and the atmosphere replaced by oxygen. To the reaction mixture was added (MeCN)₂PdCl₂ (5.0 mg, 0.019 mmol). After being stirred at room temperature for 2 h, the reaction mixture was filtered through a short pad of silica gel eluting with EtOAc and concentrated. Analysis by ¹H NMR using mesitylene (25.0 μL, 0.180 mmol, 0.900 equiv) as an internal standard indicated 69% yield. The residue was purified by silica gel column chromatography (hexane/EtOAc = 9:1) to give 2a (37.1 mg, 64%) as a colorless oil.

**Dihydropyrrone 4.** To a solution of 1 (50.0 mg, 0.194 mmol) and allyl alcohol (0.125 mL, 1.94 mmol) in DME (1 mL) was added Pd(OOCOCF₃)₂ (6.4 mg, 0.019 mmol) at room temperature under an argon atmosphere. After being stirred at room temperature for 24 h, the reaction mixture was filtered through a short pad of silica gel eluting with EtOAc and concentrated. The residue was purified by silica gel column chromatography (hexane/EtOAc = 4:1) to give 4 (34.6 mg, 69%) as a colorless oil. IR (KBr) νmax (cm⁻¹) 2958, 2929, 1667, 1604, 1399; ¹H NMR (CDCl₃, 400 MHz) δ (ppm) 7.33–7.17 (5H, m, Ph), 5.32 (1H, s, COCH₂–), 4.33 (1H, m, OCH–), 2.90–2.71 (2H, m, PhCH₂–), 2.50–2.10 (5H, m, COCH₂–, n-PrCH₂–, PhCH₂CH₂H–), 1.95 (1H, m, PhCH₂CH₂H–), 1.62–1.51 (2H, m, CH₂CH₂CH₂–), 1.44–1.31 (2H, m, CH₂CH₂CH₂–), 0.940 (3H, t, J = 7.5 Hz, CH₃–); ¹³C NMR (CDCl₃, 100 MHz) δ (ppm) 192.9, 177.7, 140.8, 128.5, 128.4, 126.2, 104.1, 78.1, 41.0, 36.0, 34.5, 31.1, 28.5, 22.2, 13.8; HRMS (ESI, positive): calcd for C₁₇H₂₆O₂Na (M + Na), 321.1825; found, 321.1827.

**Cascade Wacker/Mizoroki–Heck Reaction (Scheme 2; Table 1, Entry 1).** Aldehyde 3. To a solution of 1 (50.0 mg, 0.194 mmol) and allyl alcohol (0.125 mL, 1.94 mmol) in DME (1 mL) were added LiBr (67.4 mg, 0.776 mmol) and Cu(OAc)₂·H₂O (3.9 mg, 0.019 mmol) at room temperature under an argon atmosphere. The vessel was then degassed and the atmosphere replaced by oxygen. To the reaction mixture was added (MeCN)₂PdCl₂ (5.0 mg, 0.019 mmol). After being stirred at room temperature for 2 h, the reaction mixture was filtered through a short pad of silica gel eluting with EtOAc and concentrated. Analysis by ¹H NMR using mesitylene (25.0 μL, 0.180 mmol, 0.900 equiv) as an internal standard indicated 72% yield. The residue was purified by silica gel column chromatography (hexane/EtOAc = 3:1) to give 3 (41.0 mg, 67%) as a colorless oil. IR (KBr) νmax (cm⁻¹) 2956, 2929, 1722, 1660, 1601, 1390; ¹H NMR (CDCl₃, 400 MHz) δ (ppm) 9.76 (1H, br s, CHO–), 7.34–7.16 (5H, m, Ph), 4.23 (1H, m, OCH–), 2.88–2.68 (2H, m, PhCH₂–), 2.59–2.30 (8H, m, CHOCH₂CH₂–, CHOCH₂CH₂–, COCH₂–, n-PrCH₂–), 2.12 (1H, m, PhCH₂CH₂H–), 1.92 (1H, m, PhCH₂CH₂H–), 1.63–1.52 (2H, m, CH₃CH₂CH₂–), 1.44–1.32 (2H, m, CH₃CH₂CH₂–), 0.952 (3H, t, J = 7.5 Hz, CH₃–); ¹³C NMR (CDCl₃, 100 MHz) δ (ppm) 202.2, 192.3, 174.0, 140.9, 128.5, 128.4, 126.2, 112.9, 77.0, 43.8, 41.3, 36.1, 31.8, 31.1, 29.1, 22.6, 17.5, 13.9; HRMS (ESI, positive): calcd for C₂₀H₂₀O₃ (M + H), 315.1955; found, 315.1956.
Dihydropyrone 2c. To a solution of 1 (50.0 mg, 0.194 mmol) and 2-methyl-3-buten-2-ol (0.200 mL, 1.94 mmol) in DME (1 mL) was added (MeCN)2PdCl2 (5.0 mg, 0.019 mmol) at room temperature under an argon atmosphere. After being stirred at room temperature for 1.5 h, the reaction mixture was filtered through a short pad of silica gel eluting with EtOAc and concentrated. The residue was purified by silica gel column chromatography (hexane/EtOAc = 10:1) to give 2c (32.3 mg, 51%) as a colorless oil. IR (KBr) νmax (cm−1) 2958, 2928, 2865, 1602, 1387; 1H NMR (CDCl3, 400 MHz) δ (ppm) 7.33–7.17 (5H, m, Ph, 4.94 (1H, tt, J = 1.5, 8 Hz, MeC=C−CH−), 4.24 (1H, m, OCH−), 2.98–2.69 (4H, m, MeC=CHCH2C−, PhCH2−), 2.55–2.24 (4H, m, COCH2−, n-PrCH−), 2.11 (1H, m, PhCH2CH2H−), 1.92 (1H, m, PhCH2CH3H−), 1.69 (3H, s, CH3CH2C−CH−), 1.66 (3H, d, J = 1.5 Hz, CH3CH2C−CH−), 1.63–1.52 (2H, m, CH2CH2CH−), 1.44–1.31 (2H, m, CH2CH2CH2−), 0.947 (3H, t, J = 7.5 Hz, CH3−), 13C NMR (CDCl3, 100 MHz) δ (ppm) 192.1, 173.8, 141.0, 131.0, 128.5, 128.4, 126.1, 123.2, 114.3, 76.9, 41.4, 36.2, 31.8, 31.1, 29.0, 25.6, 22.7, 22.6, 17.8, 13.9; HRMS (ESI, positive): calcld for C21H28O2Na (M + Na), 349.2138; found, 349.2141.

Dihydrofuran 5. To a solution of 1 (50.0 mg, 0.194 mmol) and prenyl alcohol (0.200 mL, 1.94 mmol) in DME (1 mL) was added (MeCN)2PdCl2 (5.0 mg, 0.019 mmol) at room temperature under an argon atmosphere. After being stirred at room temperature for 4 h, the reaction mixture was filtered through a short pad of silica gel eluting with EtOAc and concentrated. The residue was purified by silica gel column chromatography (hexane/EtOAc = 12:1) to give 5 (80 mg, 13%) as a colorless oil. IR (KBr) νmax (cm−1) 2958, 2929, 2962, 1559, 1375; 1H NMR (CDCl3, 400 MHz) δ (ppm) 7.32–7.16 (5H, m, Ph), 7.11 (1H, td, J = 1, 16 Hz, CCH=C−), 6.59 (1H, td, J = 7, 16 Hz, CCH−), 4.88–4.83 (2H, m, CH2C−), 4.50 (1H, dd, J = 9, 10 Hz, OCH2−), 4.19 (1H, dd, J = 4.5, 9 Hz, OCH2−), 3.89 (1H, dd, J = 4.5, 10 Hz, OCH2−), 2.78 (2H, m, CH=C−), 2.59–2.50 (2H, m, PhCH2C−), 2.40 (2H, m, J = 7 Hz, COCH2−), 1.71 (3H, s, CH3−), 1.60–1.50 (2H, m, CH2CH2CH2−), 1.36–1.24 (2H, m, CH2CH2CH3−), 0.898 (3H, t, J = 7 Hz, CH3−); 13C NMR (CDCl3, 100 MHz) δ (ppm) 198.2, 164.0, 145.6, 141.8, 141.3, 128.40, 128.35, 126.0, 120.0, 113.3, 112.7, 75.1, 50.7, 40.9, 34.93, 34.90, 26.1, 22.4, 19.2, 14.0; HRMS (ESI, positive): calcld for C22H29O2 (M + H), 325.2162; found, 325.2165.

7-(Triisopropylsilyl)oxyhept-3-yn-2-one. To a solution of 1-(triisopropylsilyl)oxy-4-pentene (1.75 g, 7.28 mmol) in THF (14 mL) was added n-BuLi (1.6 M in hexane, 5.0 mL, 8.0 mmol) at −78 °C under an argon atmosphere. The reaction mixture was stirred at −78 °C for 1 h. To the reaction mixture was added 4-acetylmorphine (0.930 mL, 8.04 mmol) at −78 °C, and the resulting mixture was allowed to warm to 0 °C. The reaction was quenched with a saturated aqueous solution of NH4Cl at 0 °C. The aqueous layer was extracted with Et2O. The organic layer was dried over anhydrous Na2SO4 and concentrated. The residue was purified by silica gel column chromatography (hexane/Et2O = 20:1) to give 7-(triisopropylsilyl)oxyhept-3-yn-2-one (1.45 g, 70%) as a colorless oil. IR (KBr) νmax (cm−1) 2924, 2867, 2211, 1681, 1110; 1H NMR (CDCl3, 400 MHz) δ (ppm) 3.77 (2H, t, J = 6 Hz, TIPSOC2−), 2.49 (2H, t, J = 7 Hz, TIPSOCH2C−), 2.31 (3H, s, CH3−), 1.84–1.75 (2H, m, TIPSOCH2C−), 1.14–1.02 (21H, m, TIPS); 13C NMR (CDCl3, 100 MHz) δ (ppm) 184.8, 93.9, 81.4, 61.4, 32.7, 30.9, 18.0, 15.4, 11.9; HRMS (ESI, positive): calcld for C36H71O2Si (M + H), 528.2088; found, 528.2094.

Hydroxy Ynone 6. To a solution of disopropylamine (0.76 mL, 5.4 mmol) in THF (7.6 mL) was added n-BuLi (1.6 M in hexane, 3.4 mL, 5.4 mmol) at 0 °C under an argon atmosphere. The reaction mixture was stirred at 0 °C for 10 min. To the reaction mixture was added a solution of 7-(triisopropylsilyl)oxyhept-3-yn-2-one (1.45 g, 5.00 mmol) in THF (10 mL) at −78 °C. After being stirred at −78 °C for 2 h, a solution of 3-phenylpropanal (0.60 mL, 4.6 mmol) in THF (45 mL) was added dropwise to the resulting mixture. After being stirred at −78 °C for 15 min, the reaction was quenched with a saturated aqueous solution of NH4Cl at −78 °C, and the resulting mixture was allowed to warm to room temperature. The
aqueous layer was extracted with Et<sub>2</sub>O. The organic layer was dried over anhydrous Na<sub>2</sub>SO<sub>4</sub> and concentrated. The residue was purified by silica gel column chromatography (hexane/ Et<sub>2</sub>O = 3:1) to give 6 (1.38 g, 72%) as a colorless oil. IR (KBr) ν<sub>max</sub> (cm<sup>-1</sup>) 3455, 2943, 2866, 2213, 1671, 1109; 1<sup>H</sup> NMR (CDCl<sub>3</sub>, 400 MHz) δ (ppm) 7.32−7.16 (SH, m, Ph), 4.12 (1H, m, HOCH<sub>2</sub>−), 3.76 (2H, t, J = 6 Hz, TIPSOCH<sub>2</sub>−), 2.87−2.64 (SH, m, COCH<sub>2</sub>−, PhCH<sub>2</sub>−, OH), 2.51 (2H, t, J = 7 Hz, TIPSOCH<sub>2</sub>CH<sub>2</sub>H), 1.89−1.66 (4H, m, PhCH<sub>2</sub>CH<sub>2</sub>−, TIPSOCH<sub>2</sub>−), 1.16−1.00 (2H, m, TIPS); 1<sup>3</sup>C NMR (CDCl<sub>3</sub>, 100 MHz) δ (ppm) 186.7, 141.6, 128.5, 128.4, 126.0, 81.3, 67.3, 66.7, 52.3, 31.2, 29.6; HRMS (ESI, positive): calcd for C<sub>19</sub>H<sub>18</sub>O<sub>2</sub>Na (M + Na), 349.1244; found, 349.1259.

**Dihydropyrone 7.** To a solution of 6 (81.0 mg, 0.194 mmol) and allyl alcohol (0.125 mL, 1.94 mmol) in DME (1 mL) was added (MeCN)<sub>2</sub>PDCl<sub>3</sub> (5.0 mg, 0.019 mmol) at 0 °C under an argon atmosphere. After being stirred at room temperature for 1 h, the reaction mixture was filtered through a short pad of silica gel eluting with EtOAc and concentrated. The residue was purified by silica gel column chromatography (hexane/ EtOAc = 8:1) to give 7 (34.0 mg, 55%) as a yellow oil. IR (KBr) ν<sub>max</sub> (cm<sup>-1</sup>) 2924, 1665, 1591, 1378, 1141; 1<sup>H</sup> NMR (CDCl<sub>3</sub>, 400 MHz) δ (ppm) 3.81−3.67 (SH, m, Ph), 3.73−3.51 (SH, m, Ph), 5.91 (1H, m, CH<sub>2</sub>−CH(CH<sub>3</sub>H)−), 5.04−4.89 (2H, m, CH<sub>2</sub>−CH(CH<sub>3</sub>H)−), 4.52 (1H, m, OCH−), 3.12 (1H, m, CH<sub>2</sub>−CH(CH<sub>3</sub>H)<sub>2</sub>−), 2.97−2.77 (3H, m, CH<sub>2</sub>−CH(CH<sub>3</sub>H)<sub>2</sub>−, PhCH<sub>2</sub>−), 2.69 (1H, dd, J = 14, 16.5 Hz, COCH<sub>2</sub>H−), 2.55 (1H, dd, J = 3, 16.5 Hz, COCH<sub>2</sub>H−), 2.24 (1H, m, PhCH<sub>2</sub>CH<sub>2</sub>H−), 2.02 (1H, m, PhCH<sub>2</sub>CH<sub>2</sub>H−); 1<sup>3</sup>C NMR (CDCl<sub>3</sub>, 100 MHz) δ (ppm) 192.8, 169.1, 140.8, 137.0, 134.2, 130.4, 128.6, 128.5, 128.4, 128.2, 114.7, 113.0, 77.9, 41.6, 36.2, 31.2, 29.6; HRMS (ESI, positive): calcd for C<sub>22</sub>H<sub>22</sub>O<sub>2</sub>Na (M + Na), 341.1512; found, 341.1500.

**Hydroxy Ynone 8.** To a solution of diisopropylamine (0.76 mL, 5.4 mmol) in THF (7.6 mL) was added n-BuLi (1.6 M in hexane, 3.4 mL, 5.4 mmol) at 0 °C under an argon atmosphere. The reaction mixture was stirred at −78 °C for 10 min. To the reaction mixture was added a solution of 4-trimethylsilyl)but-3-yn-2-one (0.60 mL, 5.0 mmol) in THF (10 mL) at −78 °C. After being stirred at −78 °C for 2 h, a solution of 3-phenylpropanal (0.60 mL, 4.5 mmol) in THF (45 mL) was added dropwise to the resulting mixture. After being stirred at −78 °C for 15 min, the reaction was quenched with a saturated aqueous solution of NH<sub>4</sub>Cl at −78 °C, and the resulting mixture was allowed to warm to room temperature. The aqueous layer was extracted with Et<sub>2</sub>O. The organic layer was dried over anhydrous Na<sub>2</sub>SO<sub>4</sub> and concentrated. The residue was purified by silica gel column chromatography (hexane/ EtOAc = 7:1 to 3:1) to give 8 (186 mg, 14%) as a colorless oil and 12 (302 mg, 30%) as a colorless oil: IR (KBr) ν<sub>max</sub> (cm<sup>-1</sup>) 3446, 2958, 2925, 1726, 1243, 1217; 1H NMR (CDCl<sub>3</sub>, 400 MHz) δ (ppm) 7.38−7.30 (2H, m, Ph), 4.13 (1H, m, HOCH−), 2.87−2.61 (2H, m, PhCH<sub>2</sub>−, COCH<sub>2</sub>H), 1.95−1.66 (2H, m, PhCH<sub>2</sub>−), 0.244 (9H, s, CH<sub>3</sub>); 1<sup>3</sup>C NMR (CDCl<sub>3</sub>, 100 MHz) δ (ppm) 187.2, 141.6, 128.5 (two carbons), 125.9, 101.8, 99.3, 66.7, 52.2, 37.9, 31.7, −0.8; HRMS (ESI, positive): calcd for C<sub>19</sub>H<sub>21</sub>O<sub>2</sub>SiNa (M + Na), 329.0742; found, 329.0741.

**Dihydropyrone 9.** To a solution of 8 (54.0 mg, 0.194 mmol) and allyl alcohol (0.125 mL, 1.94 mmol) in DME (1 mL) was added (MeCN)<sub>2</sub>PDCl<sub>3</sub> (5.0 mg, 0.019 mmol) at 0 °C under an argon atmosphere. After being stirred at 0 °C for 6 h, the reaction mixture was filtered through a short pad of silica gel eluting with EtOAc and concentrated. The residue was purified by silica gel column chromatography (hexane/ EtOAc = 9:1) to give 9 (34.7 mg, 57%) as a colorless oil. IR (KBr) ν<sub>max</sub> (cm<sup>-1</sup>) 2952, 1726, 1243, 1217; 1<sup>H</sup> NMR (CDCl<sub>3</sub>, 400 MHz) δ (ppm) 7.34−7.18 (SH, m, Ph), 5.77 (1H, m, CH<sub>2</sub>−CH(CH<sub>3</sub>H)<sub>2</sub>−), 5.03−4.91 (2H, m, CH<sub>2</sub>−CH(CH<sub>3</sub>H)<sub>2</sub>−), 4.42 (1H, m, OCH−), 3.43−3.31 (2H, m, CH<sub>2</sub>−CH(CH<sub>3</sub>H)<sub>2</sub>−), 2.91−2.67 (3H, m, PhCH<sub>2</sub>−, COCH<sub>2</sub>H−), 2.34 (1H, dd, J = 7.5, 18 Hz, COCH<sub>2</sub>H−), 2.10−1.88 (2H, m, PhCH<sub>2</sub>CH<sub>2</sub>−).
To a solution of 12 (39.2 mg, 0.194 mmol) and allyl alcohol (0.125 mL, 1.94 mmol) in DME (1 mL) was added formalin (1.4 mL) at room temperature. After being stirred at 0 °C for 2 h, the reaction mixture was quenched with a saturated aqueous solution of NaHCO₃ at 0 °C under an argon atmosphere. The reaction mixture was filtered through a short pad of silica gel and washed with Et₂O. The organic layer was dried over anhydrous Na₂SO₄ and concentrated. The residue was purified by silica gel column chromatography (hexane/EtOAc = 9:1) to give 15 (28.2 mg, 75%) as a colorless oil. IR (KBr) ν_max (cm⁻¹) 2920, 2927, 1665, 1002, 1376; ¹H NMR (CDCl₃, 400 MHz) δ (ppm) 5.78 (1H, m, CH₂=CHCH₂C=C−), 5.00–4.91 (2H, m, CH₂=CHCH₂C=C−), 4.38 (4H, t, J = 6.5 Hz, OCH₂−), 2.99 (2H, d, J = 6.5 Hz, CH₂=CHCH₂C=C−), 2.55 (2H, t, J = 7 Hz, COCH₂−), 2.30 (2H, t, J = 7.5 Hz, n-PrCH₂−), 1.59–1.49 (2H, m, CH₂CH₂CH₂−), 1.40–1.29 (2H, m, CH₂CH₂CH₂−), 0.916 (3H, t, J = 7.5 Hz, CH₃−); ¹³C NMR (CDCl₃, 100 MHz) δ (ppm) 191.3, 174.7, 136.4, 114.1, 112.7, 67.2, 36.0, 31.7, 28.8, 27.9, 22.6, 13.8; HRMS (ESI, positive): calculated for C₁₉H₂₆O₂SiNa (M + Na): 321.1199; found, 321.126.

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Copies of NMR spectra for new compounds (PDF)

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Notes

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ADDITIONAL NOTE

"Lu and co-workers reported the related allylation of an arylpalladacycle complex with allylic alcohol. Further, in AcOH, the addition of LiCl favors β-OH-elimination over β-H-elimination. For details, see ref 5d.

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