Tetrahedron 65 (2009) 1794–1798

Contents lists available at ScienceDirect

Tetrahedron

journal homepage: www.elsevier.com/locate/tet

Gold(I)-catalyzed hydration of allenes

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ARTICLE INFO

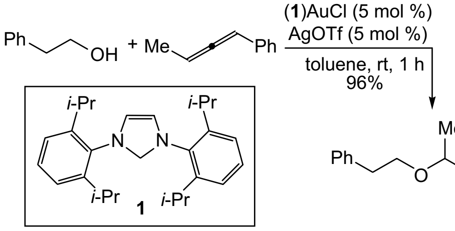
Article history:
Received 1 August 2008
Received in revised form 15 October 2008
Accepted 23 October 2008
Available online 24 December 2008

ABSTRACT

A gold(I) *N*-heterocyclic carbene complex catalyzes the intermolecular hydration of allenes to form allylic alcohols in modest yield with selective delivery of water to the terminal carbon atoms of the allenyl moiety.

1. Introduction

There has been considerable interest in the transition metal-catalyzed hydration of alkenes as an alternative to acid-catalyzed or heavy metal-mediated approaches to hydration, particularly as a means to achieve anti-Markovnikov addition.[1] However, effective transition metal-catalyzed hydration of simple alkenes has not been realized. Complexes of a number of transition metals including Pt(II),[2,3] Hg(II),[3,4] Au(I),[5] and Ru(II)[6] catalyze the hydration of alkynes,[7] but these methods are not effective for alkenes. Palladium(II) salts promote the addition of water to ethylene and unactivated 1-alkenes, but facile β-hydride elimination leads to oxidation and formation of ketones.[8] Reports on platinum-catalyzed anti-Markovnikov hydration of 1-hexene[9] have not been validated,[10] and as such transition metal-catalyzed alkene hydration has been restricted to electron deficient alkenes such as maleate esters.[11]



(1)

We became interested in the transition metal-catalyzed hydration of allenes, which are destabilized by ~10 kcal/mol relative to alkenes,[12] as an entry point into the development of catalytic alkene hydration processes. Although a number of O–H nucleophiles undergo efficient transition metal-catalyzed intermolecular addition across the C=C bond of an allene,[13,14] water is not among them. In a lone example, the Ru(II)-catalyzed reaction of monosubstituted allenes with water led to competitive hydrative dimerization and hydration initiated via attack of water at the internal allenyl carbon atom.[15] Attack of water at the central carbon of the allene is also observed in the Brønsted acid-catalyzed hydration of allenes.[16] Here we report the gold(I)-catalyzed hydration of allenes to form allylic alcohols via selective attack of water at the terminal allenyl carbon atoms.

2. Results and discussion

We have recently reported that a mixture of the gold(I) *N*-heterocyclic carbene complex (**1**)AuCl [**1**=1,3-bis(2,6-diisopropylphenyl)imidazol-2-ylidine] and AgOTf catalyzes the intermolecular hydroalkoxylation of allenes with alcohols (Eq. 1),[14] and we considered that this catalyst system might also be effective for the hydration of allenes. However, direct application of the catalyst system employed for the intermolecular hydroalkoxylation of allenes met with modest success. Stirring a mixture of 2,3-pentadienyl benzoate (**2**, 0.4 M), water (2 equiv), and a catalytic 1:1 mixture of (**1**)AuCl and AgOTf in toluene at 23 °C for 24 h led to complete consumption of **2** to form a 1:1 mixture of secondary allylic alcohols **3a** and **3b** in 33% combined yield (Table 1, entry 1). Neither 3-propanonyl benzoate, resulting from attack of water at the central allenyl carbon atom, nor 1-vinyl-1-propenyl benzoate, formed via isomerization of **2**,[17] was detected in the crude reaction mixture. Rather, the major byproducts of the gold(I)-catalyzed hydration of **2** were bis(allylic) ethers formed via sequential hydration/hydroalkoxylation. This observation suggested that inefficient hydration of **2** was due, at least in part, to the limited solubility of water in toluene. Indeed, gold(I)-catalyzed hydration of **2** in water miscible solvents such as acetone, THF, or dioxane led to significant increase in the yield of **3** (Table 1, entries 2–4). In a preparative-scale experiment, reaction of **2** (0.4 M) with water (2 equiv) and a catalytic 1:1 mixture of (**1**)AuCl and AgOTf in dioxane at 23 °C for 3 h led to isolation of **3a** in 48% yield and **3b** in 25% yield (Table 2, entry 1). Control experiments

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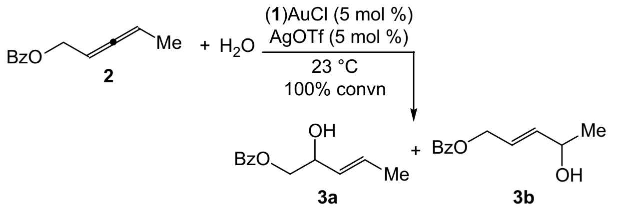
doi:10.1016/j.tet.2008.10.113

Table 1

Effect of solvent on the hydration of **2** catalyzed by a mixture of (**1**)AuCl and AgOTf



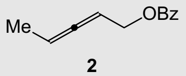
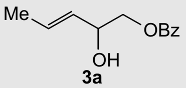
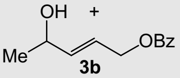
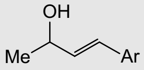
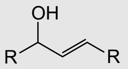
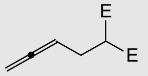
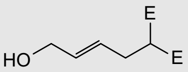
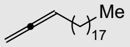
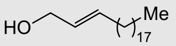
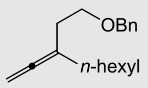
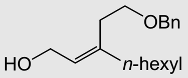
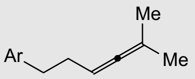
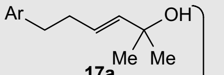
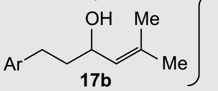
Entry	Solvent	Time (h)	Yield[a] (%)	**3a**/**3b**
1	Toluene	24	33	1:1
2	Acetone	4	69	3:1
3	THF	4	75	1:1
4	Dioxane	4	77	2:1

[a] Combined yield of **3a** and **3b** determined by GC analysis of the crude reaction mixture.

revealed that both AgOTf and (**1**)AuCl were required for allene hydration and that Brønsted acid played no role in allene hydration (see Experimental section).

Table 2

Hydration of allenes catalyzed by a mixture of (**1**)AuCl (5 mol %) and AgOTf (5 mol %) in dioxane at 23 °C

Entry	Allene	Allylic alcohol(s)	Yield[a] (%)
1	 **2**	 **3a** +  **3b**	48 25
2	 Ar=Ph (**4**)	 **6**	64[b]
3	Ar=p-$C_6H_4CF_3$ (**5**)	**7**	62
4	 **8** (R = *n*-pentyl)	 **9**	54
5	 **10** (E = CO_2Me)	 **13**	41
6	 **11**	 **14**	42
7	 **12**	 **15**	36
8	 **16** (Ar = 2-C_6H_4OBn)	 **17a** +  **17b**	73 (2.5:1)

[a] Yield refers to isolated material of >95% purity.

[b] Employment of enantiomerically enriched **4** (78% ee) led to the formation of racemic **6**.

In comparison to **2**, 1-aryl-2,3-butadienes **4** and **5** underwent gold(I)-catalyzed hydration to form **6** and **7**, respectively, in >60% yield as single regioisomers resulting from attack of water at the methyl-bound allenyl carbon atom (Table 2, entries 2 and 3). Gold(I)-catalyzed hydration of enantiomerically enriched **4** (78% ee) formed racemic **6**, owing to the rapid racemization of **4** under reaction conditions.[14,18] The 1,3-dialkyl-substituted allene **8** also underwent gold(I)-catalyzed hydration to form **9** in 54% yield (Table 2, entry 4). Gold(I)-catalyzed hydration of the monosubstituted allenes **10** and **11** and the 1,1-disubstituted allene **12** led to isolation of primary allylic alcohols **13**–**15**, respectively, as single regio- and diastereoisomer, in modest yield (Table 2, entries 5–7). In comparison, hydration of the trisubstituted allene **16** led to isolation of a 2.5:1 mixture of tertiary allylic alcohol **17a** and secondary allylic alcohol **17b**, in 73% combined yield (Table 2, entry 8).

In summary, we have developed a gold(I)-catalyzed protocol for the hydration of allenes to form (*E*)-allylic alcohols via selective delivery of water to the terminal allenyl carbon atom(s). We continue to work toward the development of more effective allene hydration catalysts and toward the development of alkene hydration catalysts.

3. Experimental

3.1. General methods

Reactions were performed under a nitrogen atmosphere employing standard Schlenk and dry box techniques unless specified otherwise. NMR spectra were obtained on Varian spectrometers operating at 400 MHz for ^{1}H NMR and 101 MHz for ^{13}C NMR in $CDCl_3$ at 25 °C unless noted otherwise. IR spectra were obtained on a Nicolet Avatar 360-FT IR spectrometer. Gas chromatography was performed on a Hewlett–Pakard 5890 gas chromatography equipped with a 15 m or 25 m polydimethylsiloxane capillary column and FID detector. Column chromatography was performed employing 230–400 mesh silica gel (Silicycle). Catalytic reactions were performed in sealed glass tubes under an atmosphere of dry nitrogen unless noted otherwise. Elemental analyses were performed by Complete Analysis Laboratories (Parsippany, NJ). Thin layer chromatography (TLC) was performed on silica gel 60 F_{254} (EMD Chemicals Inc.). Room temperature is 23 °C. All solvents were purchased from Aldrich or Acros in anhydrous form and used as received. All reagents were purchased from major suppliers and used as received. Tridec-7-yn-6-ol,[19] *o*-nitrobenzenesulfonyl hydrazine,[20] ethyl 3-hexyl-3,4-pentadienoate,[21] 4-(4-(trifluoromethyl)phenyl)-3-butyn-2-ol,[22] 2,3-pentadienyl benzoate (**2**),[14] 1-phenyl-1,2-butadiene (**4**),[14] dimethyl 2-(2,3-butadienyl)malonate (**10**),[14] and 1-(benzyloxy)-2-(5-methyl-3,4-hexadienyl)benzene (**16**)[14] were prepared employing the published procedures.

3.2. Preparation of allenes

3.2.1. 1-(1,2-Butadienyl)-4-(trifluoromethyl)benzene (5)

Diethylazodicarboxylate (1.4 mL, 8.8 mmol) was added to a solution of triphenylphosphine (2.3 g, 8.8 mmol) in THF (15 mL) at −10 °C over 1 min. The resulting solution was stirred at −10 °C for 10 min, treated with a solution of 4-(4-(trifluoromethyl)phenyl)-3-butyn-2-ol (1.45 g, 6.8 mmol) in THF (10 mL), stirred for 10 min, and treated with a solution of *o*-nitrobenzenesulfonyl hydrazine (1.9 g, 8.8 mmol) in THF (15 mL). The resulting mixture was stirred between −10 °C and 0 °C for 2 h, warmed to room temperature, and stirred overnight. The reaction mixture was cooled to 0 °C, diluted with Et_2O, washed with ice water, dried ($MgSO_4$), and concentrated. The resulting residue was chromatographed (hexane) to give **5** as a colorless oil, 74%. TLC (hexane): R_f=0.69. ^{1}H NMR: δ 7.54 (d, J=8.0 Hz, 2H), 7.38 (d, J=8.0 Hz, 2H), 6.14–6.10 (m, 1H), 5.61 (quintet, J=7.0 Hz, 1H), 1.81 (ddd, J=1.2, 3.2, 7.2 Hz, 3H). ^{13}C{^{1}H}

NMR: δ 207.1, 139.3, 128.8 (q, $^{2}J_{C-F}$=32.4 Hz), 126.9, 125.7 (q, $^{3}J_{C-F}$=4.0 Hz), 124.5 (q, $^{1}J_{C-F}$=271.9 Hz), 93.2, 90.2, 13.8. IR (neat, cm^{-1}): 2930, 1615, 1322, 1162, 1119, 1064, 1016, 875, 843, 754. HRMS calcd (found) for $C_{11}H_{9}F_{3}$ (M^{+}): 198.0656 (198.0657).

3.2.2. *6,7-Tridecadiene (**8**)*

6,7-Tridecadiene (**8**)[23] was synthesized from tridec-7-yn-6-ol (0.30 g, 1.5 mmol) employing a procedure analogous to that used to synthesize **5**. Colorless oil, 37%. ^{1}H NMR: δ 5.09–5.04 (m, 2H), 2.00–1.94 (m, 4H), 1.45–1.25 (m, 12H), 0.89 (t, J=6.8 Hz, 6H). ^{13}C{^{1}H} NMR: δ 204.0, 91.1, 31.6, 29.2, 29.1, 22.7, 14.3.

3.2.3. *Henicosa-1,2-diene (**11**)*

1-Icosyne (5.10 g, 50.0 mmol) was added to a suspension of formaldehyde (1.55 g, 50.0 mmol), diisopropylamine (5.10 g, 50.0 mmol), and CuBr (1.44 g, 10.0 mmol) in dioxane (75 mL). The mixture was refluxed for 20 h, cooled, and concentrated under vacuum. The residue was diluted with $Et_{2}O$ (150 mL), filtered through silica gel, eluted with $Et_{2}O$ (150 mL), and the filtrate was concentrated under vacuum. Column chromatography of the residue (hexane) gave **11** (3.43 g, 52%) as a white solid. TLC (hexane): R_f=0.81. ^{1}H NMR: δ 5.06 (quintet, J=6.8 Hz, 1H), 4.61 (td, J=3.2, 6.8 Hz, 2H), 2.03–1.94 (m, 2H), 1.48–1.10 (m, 32H), 0.87 (t, J=6.8 Hz, 3H). ^{13}C{^{1}H} NMR: δ 208.7, 90.2, 74.6, 32.2, 30.0, 29.7, 29.6, 29.4, 29.3, 28.5, 22.9, 14.3. IR (neat, cm^{-1}): 2956, 2915, 2848, 1956, 1467, 861, 841, 721, 562. HRMS calcd (found) for $C_{21}H_{40}$ (M^{+}): 292.3130 (292.3127).

3.2.4. *3-(2-Benzyloxyethyl)-1,2-nonadiene (**12**)*

Ethyl 3-hexyl-3,4-pentadienoate (2.54 g, 12.9 mmol) was added dropwise to a stirred suspension of $LiAlH_{4}$ (0.63 g, 16.5 mmol) in THF (100 mL) at 0 °C. The reaction mixture was stirred for 4 h and then treated sequentially with water (0.6 mL), NaOH 15% (1.25 mL), and water (2 mL). The resulting mixture was filtered through a pad of Celite and concentrated to give 3-hexyl-3,4-pentadien-1-ol (**18**) as a colorless oil (1.93 g, 97%) that was used in the subsequent step without further purification. Alcohol **18** (1.00 g, 5.94 mmol) was added dropwise to a stirred suspension of NaH (171 mg, 7.14 mmol) in DMF (50 mL) at 0 °C, stirred for 30 min, and treated with benzyl bromide (1.22 g, 7.14 mmol). The resulting suspension was warmed to room temperature and stirred for 10 h. The reaction mixture was cooled to 0 °C, treated with water (50 mL), and extracted with EtOAc (100 mL). The combined organic extracts were washed with brine (75 mL), dried ($MgSO_{4}$), and concentrated. The resulting residue was chromatographed (hexanes–EtOAc=30:1) to give **12** as a colorless oil (0.67 g, 43%).

*For **18***:[24] TLC (hexanes–EtOAc=4:1): R_f=0.17. ^{1}H NMR: δ 4.78–4.64 (m, 2H), 3.73 (t, J=6.2 Hz, 2H), 2.23–2.17 (m, 2H), 1.99–1.88 (m, 2H), 1.81 (s, 1H), 1.52–1.20 (m, 8H), 0.87 (t, J=6.3 Hz, 3H). ^{13}C{^{1}H} NMR: δ 205.6, 100.4, 76.3, 60.9, 35.4, 32.4, 31.8, 29.1, 27.5, 22.7, 14.2. IR (neat, cm^{-1}): 3395, 2955, 2926, 2856, 1716, 1457, 1378, 1175, 1029, 845, 724. HRMS: calcd (found) for $C_{11}H_{20}O$ (M^{+}): 168.1514 (168.1516).

*For **12***: TLC (hexanes–EtOAc=4:1): R_f=0.83. ^{1}H NMR: δ 7.39–7.28 (m, 5H), 4.74–4.67 (m, 2H), 4.55 (s, 2H), 3.62 (t, J=7.0 Hz, 2H), 2.35–2.25 (m, 2H), 2.04–1.95 (m, 2H), 1.51–1.24 (m, 8H), 0.92 (t, J=6.7 Hz, 3H). ^{13}C{^{1}H} NMR: δ 205.9, 138.7, 128.4, 127.8, 127.6, 100.3, 75.8, 73.0, 68.9, 32.5, 32.3, 31.8, 29.1, 27.5, 22.8, 14.2. IR (neat, cm^{-1}): 2924, 2855, 1454, 1362, 1099, 844, 732, 696. HRMS calcd (found) for $C_{18}H_{26}O$ (M^{+}): 258.1984 (258.1982).

3.3. Hydration products

3.3.1. *(E)-4-Hydroxy-2-pentenyl benzoate (**3a**) and (E)-2-hydroxy-3-pentenyl benzoate (**3b**)*

A mixture of (**1**)AuCl (6.2 mg, 0.010 mmol) and AgOTf (2.6 mg, 0.010 mmol) in 1,4-dioxane (0.2 mL) was stirred at room temperature for 5 min, treated with a solution of **2** (37.6 mg, 0.20 mmol) and $H_{2}O$ (5.4 mg, 0.30 mmol) in 1,4-dioxane (0.3 mL), and stirred at room temperature for 4 h. Column chromatography of the crude reaction mixture (hexanes–EtOAc=10:1→2:1) gave (*E*)-4-hydroxy-2-pentenyl benzoate (**3a**, 19.8 mg, 48%) and (*E*)-2-hydroxy-3-pentenyl benzoate (**3b**, 10.1 mg, 25%) as colorless oils.

*For **3a***: TLC (hexanes–EtOAc=5:1): R_f=0.18. ^{1}H NMR: δ 8.04–8.01 (m, 2H), 7.55–7.51 (m, 1H), 7.43–7.39 (m, 2H), 5.83 (dqd, J=1.2, 6.4, 15.6 Hz, 1H), 5.53 (qdd, J=1.6, 6.4, 15.2 Hz, 1H), 4.46–4.41 (m, 1H), 4.34 (dd, J=3.8, 11.2 Hz, 1H), 4.22 (dd, J=7.2, 11.2 Hz, 1H), 2.36 (br s, 1H), 1.71–1.69 (m, 3H). ^{13}C{^{1}H} NMR: δ 166.9, 133.3, 130.1, 129.8, 129.5, 129.3, 128.6, 71.1, 68.8, 18.0. IR (neat, cm^{-1}): 3468, 2949, 1712, 1602, 1449, 1376, 1271, 1115, 1068, 967, 710. Anal. Calcd (found) for $C_{12}H_{14}O_{3}$: C, 69.88 (69.76); H, 6.84 (6.79).

*For **3b***: TLC (hexanes–EtOAc=5:1): R_f=0.09. ^{1}H NMR: δ 8.04–8.02 (m, 2H), 7.55–7.51 (m, 1H), 7.43–7.39 (m, 2H), 5.90 (dd, J=4.8, 16.0 Hz, 1H), 5.85 (td, J=5.2, 15.6 Hz, 1H), 4.79 (dd, J=1.0, 4.6 Hz, 2H), 4.37–4.31 (m, 1H), 1.89 (br s, 1H), 1.27 (d, J=6.4 Hz, 3H). ^{13}C{^{1}H} NMR: δ 166.5, 138.6, 133.2, 130.3, 129.8, 128.5, 123.8, 68.1, 64.9, 23.3. IR (neat, cm^{-1}): 3409, 2971, 1713, 1602, 1450, 1375, 1268, 1112, 1066, 967, 710. Anal. Calcd (found) for $C_{12}H_{14}O_{3}$: C, 69.88 (69.76); H, 6.84 (6.94).

The *E*-configuration of allylic alcohols was assigned on the basis of the large vicinal C=C coupling constant of the allylic moiety in the ^{1}H NMR spectrum ($^{3}J_{HH}\approx 15.6$ Hz).

3.3.2. *(E)-4-Phenyl-3-buten-2-ol (**6**)*[25]

A mixture of (**1**)AuCl (12.4 mg, 0.020 mmol) and AgOTf (5.1 mg, 0.020 mmol) in 1,4-dioxane (0.2 mL) was stirred at room temperature for 5 min, treated with a solution of buta-1,2-dienylbenzene (**4**) (52.1 mg, 0.40 mmol) and $H_{2}O$ (14.4 mg, 0.80 mmol) in 1,4-dioxane (0.3 mL), and stirred at room temperature for 3 h. Column chromatography of the crude reaction mixture (hexanes–EtOAc=10:1→5:1) gave **6** (31.9 mg, 54%) as a colorless oil. TLC (hexanes–EtOAc=5:1): R_f=0.20. ^{1}H NMR: δ 7.36–7.19 (m, 5H), 6.53 (d, J=16.0 Hz, 1H), 6.23 (ddd, J=1.2, 6.4, 16.0 Hz, 1H), 4.50–4.42 (m, 1H), 1.80 (br s, 1H), 1.34 (dd, J=1.2, 6.4 Hz, 3H). ^{13}C{^{1}H} NMR: δ 136.9, 133.8, 129.6, 128.8, 127.8, 126.6, 69.1, 23.6.

All remaining intermolecular hydration reactions were performed employing a procedure analogous to that used to synthesize **6** unless noted otherwise.

3.3.3. *(E)-4-(4-(Trifluoromethyl)phenyl)-3-buten-2-ol (**7**)*

Colorless oil, 62%. TLC ($CH_{2}Cl_{2}$): R_f=0.24. ^{1}H NMR: δ 7.54 (d, J=8.4 Hz, 2H), 7.44 (d, J=8.0 Hz, 2H), 6.59 (d, J=16.0 Hz, 1H), 6.34 (dd, J=6.0, 16.0 Hz, 1H), 4.50 (quintet, J=6.4 Hz, 1H), 1.72 (br s, 1H), 1.37 (d, J=6.4 Hz, 3H). ^{13}C{^{1}H} NMR: δ 140.5, 136.4, 129.6 (q, J=32.4 Hz), 128.1, 126.8, 125.7 (q, J=4.0 Hz), 124.4 (q, J=271.9 Hz), 68.8, 23.6. IR (neat, cm^{-1}): 3359, 2976, 1616, 1414, 1322, 1163, 1119, 1066, 816. HRMS calcd (found) for $C_{11}H_{11}F_{3}O$ (M^{+}): 216.0762 (216.0762).

3.3.4. *(E)-Tridec-7-en-6-ol (**9**)*

Colorless oil, 54%. TLC (hexanes–EtOAc=8:1): R_f=0.40. ^{1}H NMR: δ 5.63 (dt, J=6.8, 15.2 Hz, 1H), 5.44 (ddt, J=1.2, 7.2, 15.2 Hz, 1H), 4.03 (q, J=6.8 Hz, 1H), 2.02 (q, J=6.8 Hz, 2H), 1.60–1.20 (m, 15H), 0.88 (t, J=6.8 Hz, 6H). ^{13}C{^{1}H} NMR: δ 133.2, 132.5, 73.5, 37.5, 32.4, 32.0, 31.6, 29.1, 25.4, 22.8, 22.7, 14.3, 14.2. IR (neat, cm^{-1}): 2957, 2923, 2853, 1463, 1378, 1062, 969. HRMS calcd (found) for $C_{13}H_{26}O$ (M^{+}): 198.1984 (198.1977).

3.3.5. *(E)-Dimethyl 2-(4-hydroxy-2-butenyl)malonate (**13**)*

Colorless oil, 41%. TLC (hexanes–EtOAc=1:5): R_f=0.51. ^{1}H NMR: δ 5.72 (ttd, J=0.8, 5.2, 15.6 Hz, 1H), 5.63 (ttd, J=0.8, 6.8, 15.6 Hz, 1H), 4.07–4.04 (m, 2H), 3.71 (s, 6H), 3.42 (t, J=7.4 Hz, 1H), 2.62 (dt, J=0.8, 7.0 Hz, 2H), 1.53 (br s, 1H). $^{13}C\{^1H\}$ NMR: δ 169.4, 132.6, 127.6, 63.4, 52.8, 51.7, 31.6. IR (neat, cm^{-1}): 3378, 2955, 1731, 1437, 1343, 1231, 1157, 1096, 974, 851. HRMS calcd (found) for $C_9H_{12}O_4$ (M^+-H_2O): 184.0736 (184.0738).

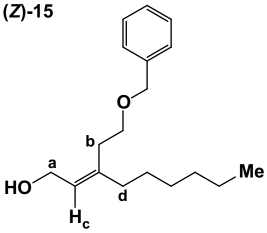
*3.3.6. (E)-2-Henicosen-1-ol (**14**)*

White solid, (42%). TLC (hexane): R_f=0.25. ^1H NMR: δ 5.69 (td, J=6.4, 15.6 Hz, 1H), 5.55 (td, J=6.4, 15.2 Hz, 1H), 3.90 (dd, J=1.2, 6.0 Hz, 2H), 2.03 (q, J=6.8 Hz, 2H), 1.50–1.00 (m, 33H), 0.88 (t, J=6.4 Hz, 3H). $^{13}C\{^1H\}$ NMR: δ 135.1, 126.5, 70.9, 32.5, 32.2, 29.9, 29.7, 29.6, 29.4, 29.3, 22.9, 14.3. IR (neat, cm^{-1}): 2955, 2917, 2871, 2848, 1712, 1471, 1462, 1375, 1360, 1260, 1166, 1118, 1064, 1019, 965, 803, 719, 599. HRMS calcd (found) for $C_{21}H_{42}O$ (M^+): 310.3236 (310.3240).

*3.3.7. (Z)-3-(2-(Benzyloxy)ethyl)-2-nonen-1-ol (**15**)*

Colorless oil, 36%. TLC (hexanes–EtOAc=5:1): R_f=0.30. ^1H NMR: δ 7.32–7.20 (m, 5H), 5.63 (t, J=7.6 Hz, 1H), 4.46 (s, 2H), 3.97 (dd, J=5.6, 7.6 Hz, 2H), 3.44 (t, J=6.0 Hz, 2H), 2.40 (t, J=5.6 Hz, 1H), 2.35 (t, J=6.0 Hz, 2H), 1.95 (t, J=6.8 Hz, 2H), 1.39–1.15 (m, 8H), 0.83 (t, J=6.8 Hz, 3H). $^{13}C\{^1H\}$ NMR: δ 141.8, 137.8, 128.7, 128.1, 126.1, 73.4, 67.8, 58.1, 36.7, 31.9, 30.9, 29.3, 28.0, 22.8, 14.3. IR (neat, cm^{-1}): 3370, 2954, 2925, 2855, 1496, 1465, 1454, 1415, 1361, 1097, 1002, 735, 697. HRMS calcd (found) for $C_{18}H_{28}O_2$ (M^+-H_2O): 258.1984 (258.1986). The *Z*-configuration of allylic alcohol (*Z*)-**15** was unambiguously assigned through NOE analysis. Irradiation of proton H_a led to enhancement of H_b but no enhancement of H_d, and irradiation of H_c led to enhancement of H_d but no enhancement of H_b.

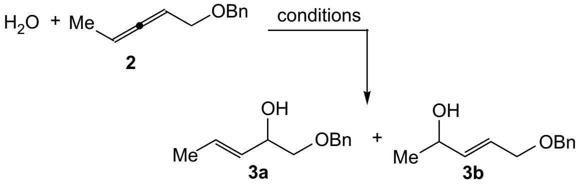
(*Z*)-15



*3.3.8. Hydration of 1-(benzyloxy)-2-(5-methyl-3,4-hexadienyl)-benzene (**16**)*

A mixture of (**1**)AuCl (6.2 mg, 0.010 mmol) and AgOTf (2.6 mg, 0.010 mmol) in 1,4-dioxane (0.2 mL) was stirred at room temperature for 5 min, treated with a solution of **16** (55.7 mg, 0.20 mmol) and H_2O (5.4 mg, 0.30 mmol) in 1,4-dioxane (0.3 mL), and stirred at room temperature for 9 h. Column chromatography of the crude reaction mixture (hexanes–EtOAc=10:1→5:1) gave a 2.5:1 mixture of (*E*)-6-(2-(benzyloxy)phenyl)-2-methyl-3-hexen-2-ol (**17a**) and 1-(2-(benzyloxy)phenyl)-5-methyl-4-hexen-3-ol (**17b**) (43.2 mg, 73%) as a colorless oil. TLC (hexanes–EtOAc=5:1): R_f=0.28. ^1H NMR (**17a**): δ 7.46–6.89 (m, 9H), 5.68 (td, J=6.4, 15.6 Hz, 1H), 5.58 (dd, J=0.8, 15.6 Hz, 1H), 5.09 (s, 2H), 2.77 (t, J=7.2 Hz, 2H), 2.35 (td, J=6.8, 8.8 Hz, 2H), 1.43 (br s, 1H), 1.27 (s, 6H). ^1H NMR (**17b**): δ 7.46–6.89 (m, 9H), 5.20 (d, J=8.8 Hz, 1H), 5.08 (s, 2H), 4.33 (q, J=7.2 Hz, 1H), 2.84–2.66 (m, 2H), 1.94–1.67 (m, 2H), 1.71 (s, 3H), 1.62 (s, 3H), 1.44 (br s, 1H). $^{13}C\{^1H\}$ NMR (both **17a** and **17b**): δ 156.7, 156.6, 138.5, 137.7, 137.5, 135.2, 130.9, 130.8, 130.3, 130.2, 128.7, 128.6, 128.2, 128.0, 127.9, 127.3, 127.25, 127.23, 127.20, 127.0, 121.1, 120.8, 111.9, 111.8, 70.7, 70.1, 69.9, 68.4, 38.1, 32.7, 30.6, 29.9, 26.5, 25.9, 18.4. IR (neat, cm^{-1}): 3350, 2969, 1596, 1494, 1451, 1377, 1236, 1112, 1022, 970, 746, 695. HRMS calcd (found) for $C_{20}H_{24}O_2$ (M^+): 296.1776 (296.1774).

3.4. Control experiments



(1) Treatment of water (5.4 mg, 0.30 mmol) and **2** (37.6 mg, 0.20 mmol) with (**1**)AuCl (5 mol %) in dioxane (0.5 mL) at 23 °C for 40 h led to no consumption of **2** as determined by GC analysis of the crude reaction mixture versus decane internal standard.

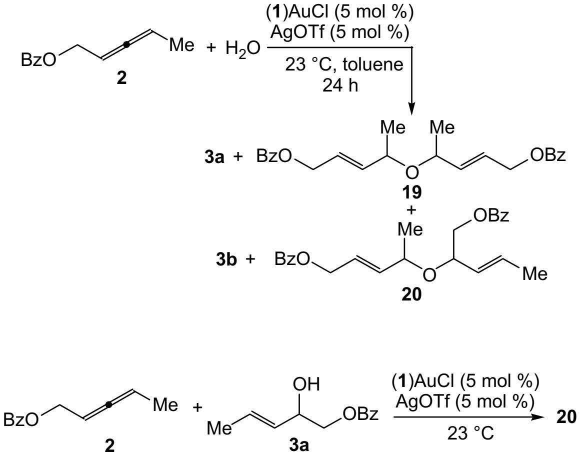
(2) Treatment of water (5.4 mg, 0.30 mmol) and **2** (37.6 mg, 0.20 mmol) with **1** (5 mol %) and AgOTf (5 mol %) in dioxane (0.5 mL) at 23 °C for 40 h led to no consumption of **2** as determined by GC analysis of the crude reaction mixture versus decane internal standard.

(3) Treatment of water (5.4 mg, 0.30 mmol) and **2** (37.6 mg, 0.20 mmol) with **1** (5 mol %) and HOTf (5 mol %) in dioxane (0.5 mL) at 23 °C for 40 h led to no consumption of **2** as determined by GC analysis of the crude reaction mixture versus decane internal standard.

(4) Treatment of water (5.4 mg, 0.30 mmol) and **2** (37.6 mg, 0.20 mmol) with HOTf (10 mol %) in dioxane (0.5 mL) at 23 °C for 40 h led to no consumption of **2** as determined by GC analysis of the crude reaction mixture versus decane internal standard.

3.5. Identification of byproducts from the reaction of water with 2

A mixture of (**1**)AuCl (18.6 mg, 0.030 mmol) and AgOTf (7.7 mg, 0.030 mmol) in dioxane (0.2 mL) was stirred at room temperature for 5 min, treated with a solution of **2** (112.8 mg, 0.6 mmol) and water (16.2 mg, 0.9 mmol) in dioxane (0.3 mL), and stirred at room temperature for 4 h. GC analysis of the crude reaction mixture revealed formation of a ~1:1 mixture of **3a** and **3b** (GC retention times=2.72 and 2.52 min, respectively) that accounted for 33% of the reaction mixture. The remainder of the reaction mixture consisted of a 1.5:1.5:1:1 mixture of four compounds that eluted at 7.24



Scheme 1.

(**19a**), 7.42 (**19b**), 7.48 (**20a**), and 7.55 (**20b**) min (Scheme 1). Column chromatography of the crude reaction mixture (hexanes–EtOAc$=15{:}1\rightarrow10{:}1$) gave one fraction that contained a 1:1 mixture of **19a** and **19b** (27 mg, 23% yield) and a second fraction that contained a 1:1 mixture of **20a** and **20b** (18 mg, 15% yield). ^{1}H NMR analysis of **19** and **20** was consistent with diastereomeric mixtures of regioisomeric diallyl ether derivatives (see below). No parent ion peak was observed for either **19** or **20** via EIMS owing to facile fragmentation about the allylic C–O bonds. Rather, key fragments observed in the EIMS were m/z=273.1 (M^+-OBz) and 189.1 [$M^+-OCH(Me)C(H){=}C(H)CH_2OBz$] (see below).

The assignment of **20** was supported through independent synthesis (Scheme 1). A mixture of (**1**)AuCl (2.2 mg, 3.6×10^{-3} mmol) and AgOTf (0.9 mg, 3.6×10^{-3} mmol) in dioxane (0.2 mL) was stirred at room temperature for 5 min, treated with a solution of **2** (13.5 mg, 0.072 mmol) and **3a** (15 mg, 0.072 mmol) in dioxane (0.3 mL), and stirred at room temperature for 12 h. Column chromatography of the crude reaction mixture (hexanes–$CH_2Cl_2=1{:}1\rightarrow1{:}2$) gave **20** (5 mg, 18%) as a 1:1 mixture of diastereomers. The GC and ^{1}H NMR spectra of **20** formed from regioselective hydroalkoxylation of **2** with **3a**[14] were identical to those of **20** isolated from the gold(I)-catalyzed hydration of **2**.

*For **19***: ^{1}H NMR: δ 8.07–8.03 (m, 4H), 7.59–7.53 (m, 2H), 7.47–7.41 (m, 4H), 5.90–5.70 (m, 4H), [4.83 (d, J=5.2 Hz), 4.80 (d, J=4.4 Hz), 1:1, 4H], [4.06 (q, J=6.4 Hz), 4.00 (q, J=6.4 Hz), 1:1, 2H], [1.25 (d, J=6.4 Hz), 1.24 (d, J=6.8 Hz), 1:1, 6H]. The EIMS displayed three major peaks at m/z=273.1 [M^+-OBz], 189.1 [$M^+-OCH(Me)C(H){=}C(H)CH_2OBz$], and 105.0 [OBz].

*For **20***: ^{1}H NMR: δ 8.07–8.02 (m, 4H), 7.59–7.49 (m, 2H), 7.46–7.36 (m, 4H), 5.90–5.70 (m, 3H), [5.45 (qdd, J=2.0, 7.2, 15.6 Hz), 5.40 (qdd, J=2.0, 7.2, 15.6 Hz), 1:1, 1H], 4.81 (m, 1H), 4.72 (d, J=5.6 Hz, 1H), [4.37–4.11 (m), 4.04 (q, J=6.8 Hz) 1:1, 4H], [1.74 (dd, J=1.6, 6.4 Hz), 1.70 (dd, J=1.6, 6.8 Hz), 1:1, 3H], [1.26 (dd, J=1.6, 6.8 Hz), 1.26 (m), 1:1, 3H]. The EIMS displayed two major peaks at m/z=189.1 [$M^+-OCH(Me)C(H){=}C(H)CH_2OBz$] and 105.0 [OBz].

Acknowledgements

Acknowledgment is made to the NSF (CHE-0555425), NIH (GM-080422), and Johnson & Johnson for support of this research.

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